Aus der Klinik für Kardiovaskuläre Chirurgie
Universitätsklinik Düsseldorf
Ärztlicher Direktor Prof. Dr. med. A. Lichtenberg

Zerebrale Komplikationen nach Herzoperationen

Neue Strategien der Risikovermeidung

Habilitationsschrift

Zur Erlangung der *Venia Legendi* für das Fach Herzchirurgie

an der
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Vorgelegt von
Dr. med. Alexander Albert
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Gewidmet meinem Vater

Professor Gerhard Albert (1935-1983)

1. INHALTSVERZEICHNIS

2. ABKÜRZUNGSVERZEICHNIS

Anaortic - ohne Berührung der Hauptschlagader (Aorta)

AQUA – Institut für Angewandte Qualitätsförderung und Foschung im Gesundheitswesen

A-S-C-O - engl: A for atherosclerosis, S for small vessel disease, C for cardiac source, O for other cause (Stroke Classification)

BQS - Bundesgeschäftsstelle Qualitätssicherung

CCS - engl: causative classification system (Stroke Classification)

COPD - engl: chronic obstructive pulmonary disease

DataMart - Datenmarkt

DataWarehouse - Datenlager

DW-MRT - Diffusions-Gewichtete Magnetresonanztomographie

EKZ - Extrakorporale Zirkulation

HITS – engl: high-intensity transient signals

HLM - Herz-Lungen-Maschine

KIS - Krankenhausinformationssystem

NHP - engl: Nottingham Health Profile (NHP)

OPCAB- engl: Off-pump coronary arteries bypass surgery

pAVK - peripher arterielle Verschlusskrankheit

POCD - engl: postoperative cognitive dysfunction

SIRS - engl: systemic inflammatory response syndrome

TKD - Transkranieller Doppler

TOAST - engl: ORG 10172 in Acute Stroke Treatment

TOPCAB – engl: Total Arterial Off-pump coronary arteries bypass surgery

VLADs - Variable Life Adjusted Displays

3. VERWENDETE ORIGINALPUBLIKATIONEN

I. Albert A, Beller C, Arnrich B, Walter J, Rosendahl U, Hetzel A, Priss H, Ennker J. Is there any impact of the type of aortic end-hole cannula on stroke occurrence? Clinical evaluation of straight and bent-tip aortic cannulae. *Perfusion* 2002;6:451-456.

II. Albert A, Beller C, Walter J, Arnrich B, Rosendahl U, Priss H, Ennker J. Preoperative high leukocyte count: a novel risk factor for stroke after cardiac surgery. *Ann Thorac Surg* 2003;75:1550-1557.

III. Albert A, Walter J, Arnrich B, Hassanein W, Rosendahl U, Bauer S, Ennker J. On-line variable live-adjusted displays with internal and external risk-adjusted mortalities. A valuable method for benchmarking and early detection of unfavourable trends in cardiac surgery. *Eur J Cardiothorac Surg* 2004;25:312-319.

IV. Albert A, Peck EA, Wouters P, Van Hemelrijck J, Bert C, Sergeant P. Performance analysis of interactive multimodal CME retraining on attitude toward and application of OPCAB. *J Thorac Cardiovasc Surg* 2006;131:154-62.

V. Albert A, Hassanein W, Florath I, Voehringer L, Abugameh A, Ennker J. Technical aspects of composite arterial T-grafts: estimation of required conduit length by a simple formula. *Thorac Cardiovasc Surg* 2008;56:461-6.

VI. Albert A, Sergeant P, Florath I, Ismael M, Rosendahl U, Ennker J. A process review of a departmental change from conventional CABG to TOPCAB (Total Arterial OPCAB) and its effect on the incidence and severity of postoperative stroke. *Heart Surg Forum 2011*;14:73-80

4. EINLEITUNG

In der vorliegenden Arbeit werden verschiedene aufeinander aufbauende Strategien zur Vermeidung perioperativer neurologischer Komplikationen vorgestellt, angefangen bei Risikofaktoranalysen des perioperativen Schlaganfalls bis zur Umstellung der konventionellen Bypassoperation auf die neue Technik des „Anaortic OPCAB“. Die hier vorgestellten sechs Publikationen markieren die wichtigsten Etappen dieser Entwicklung.

Im ersten Teil der Einleitung wird zunächst der fachliche Kontext umschrieben: Die klinischen Symptome, die aktuellen Klassifikationen, Risikofaktoren und mögliche Ursachen des herzchirurgischen Schlaganfalls werden in wesentlichen Aspekten dargestellt. Dabei wird auch erläutert, inwiefern der Entwicklung von neuen Methoden zur Senkung des postoperativen Schlaganfallrisikos derzeit für das Fachgebiet der Herzchirurgie eine ganz besondere Bedeutung zukommt.

Im zweiten Teil der Einleitung werden die strukturellen und methodischen Grundvoraussetzungen erläutert, welche zunächst geschaffen werden mussten, um diese klinischen Studien zum Schlaganfall durchzuführen. Beim Studium eines Ereignisses mit einer statistisch derart niedrigen Ereignisrate wie dem perioperativen Schlaganfall gibt es besondere Herausforderungen an die statistische Methodik und die Datenbasis. Wie bei Analysen der operativen Letalität sind auch bezüglich des perioperativen Schlaganfalls weitere Verbesserungen der Operationsergebnisse, nur noch nach Analysen großer Patientenserien objektivierbar und im klinischen Alltag für den einzelnen Chirurgen kaum oder gar nicht mehr erkennbar. Gesetzt dem Fall, dass ein neues Verfahren in der Lage wäre, die postoperative Schlaganfallrate um 50% zu senken, so würde man, bei einer Schlaganfallrate unter konventioneller Bypassoperation von 1%, nach 200 Herzoperationen *einen* Schlaganfall weniger beobachten. Entsprechend der statistischen Fallzahlberechnung bräuchte man dann im Falle einer prospektiv-randomisierten Studie 5016 Patienten in jeder Therapiegruppe, um einen signifikanten Unterschied zu sehen.

Insofern bauten wir zunächst eine besondere klinische Datenbank, einen „DataMart“ auf, der eine quantitativ und qualitativ ausreichende Datenbasis besitzt, um die Risikofaktoranalyse des perioperativen Schlaganfalls (*Publikationen I und II*) und eine interne Qualitätskontrolle mit einem kontinuierlichen Monitoring und Bewertungen operativer Einflussgrößen, zu ermöglichen (*Publikationen IV bis VI*).

4.1. ZEREBRALE KOMPLIKATIONEN

4.1.1. Schlaganfall, Delir und POCD

Herzoperationen gehen mit einer postoperativen Häufung von Hirnfunktionsstörungen einher; man unterscheidet den Schlaganfall, das Delir und die subtilen Verschlechterungen der kognitiven Leistungsfähigkeit, die als postoperative kognitive Dysfunktion bezeichnet werden („postoperative cognitive dysfunction", POCD) [Schwarz 2011].

Die in den letzten Jahrzehnten erzielten Fortschritte auf dem Gebiet der extrakorporalen Zirkulation und die sich entwickelnden Routinen in der operativen und perioperativen Therapie führten zu einer Senkung der Rate an neurologischen Komplikationen [Tarakji 2011, Borger 1998]. Gleichzeitig nahmen jedoch das Alter und das Risikoprofil der herzchirurgischen Patienten zu [Gummert 2010], so dass einige Autoren einen Wiederanstieg neurologischer Komplikationen beobachten [McKhann 2006, Baker 2001]. Im Vergleich zu allgemeinchirurgischen Operationen und interventionellen Verfahren sind die Raten an neurologischen Ereignissen in der Herzchirurgie immer noch hoch: So werden neu aufgetretene fokal-neurologisches Defizite in 0,6%-10%, Hirnorganische Psychosyndrome in 8,4%-32% und neurokognitive Veränderungen in 20%-30% der Patienten beobachtet [Selim 2007, Hogue 2008, McKhann 2006, Sergeant 2004, Newman 1996, Tarakji 2011]. Die enorme Schwankungsbreite der Angaben erklärt sich durch das Risikoprofil der Patienten und die Operationsart, vor allem aber auch durch eine unterschiedliche Intensität der postoperativen neurologischen Überwachung und die Sensitivität der Diagnostik. Unterschiede in der Häufigkeit des Auftretens zerebraler Komplikationen spiegeln wahrscheinlich auch Unterschiede in der Behandlungsqualität zwischen den Kliniken wieder. Daher wird der Parameter *„Seltenes Auftreten einer postoperativen zerebrovaskulären Komplikation (TIA, Schlaganfall oder Koma)"* als ein Qualitätsindikator in der externen Qualitätssicherung Herzchirurgie und für das Klinik-Ranking verwendet [http://www.sqg.de]

Die typischen Symptome des *perioperativen Schlaganfalls* sind Halbseitenschwäche, Sprach- und Sprechstörungen, und Sehstörungen wie monookuläre Blindheit, Hemianopsie, und Doppelbilder [Baker 2001]. Das Risiko einen Schlaganfall zu erleiden, ebbt mit dem zeitlichen Abstand zur Operation ab und erreicht nach ca. 2 Wochen das für die jeweilige Patientengruppe normale Basis-Schlaganfallrisiko [Tarakji 2011, Hogue 1999, Sergeant 2004].

Die Patienten können bereits in der Aufwachphase nach der Operation durch fokale oder generalisierte Krampfanfälle oder durch ein verzögertes und inadäquates Aufwachen aus der Narkose auffallen.
Ein *postoperatives Delir* zeigt sich klassischerweise durch Bewusstseinsstörungen, Desorientierung, Halluzinationen oder eine massive Einschränkung intellektueller Leistungen [Schwarz 2011].
Die neuropsychologischen Veränderungen des POCD dagegen betreffen vorrangig die deklarativen Gedächtnis- und Exekutivfunktionen und lassen sich mit Hilfe spezieller Testverfahren identifizieren. Im klinischen Alltag fällt das POCD kaum auf; typischerweise werden die zerebralen Funktionseinschränkungen des POCD in komplexen Anforderungen des normalen Lebens bemerkbar, so beispielsweise beim Autofahren, wo sie zu einer verminderten Aufmerksamkeit führen können [Ahlgren 2003]. Während ein postoperatives Delir definitionsgemäß transient ist und Patienten nur in der frühpostoperativen Phase betrifft, so bleibt ein POCD über Monate manchmal Jahre bestehen [Schwarz 2011].
In den hier vorgestellten Originalarbeiten werden als neurologische Komplikation explizit nur der Schlaganfall, nicht jedoch das Delir und das POCD behandelt. An der Pathogenese des POCD sind wahrscheinlich ähnliche Mechanismen wie bei Schlaganfällen beteiligt: wie beim Schlaganfall werden auch für die Genese des POCD in erster Linie aortale oder kardiale Hirnembolien diskutiert; der Unterschied zur Pathogenese des Schlaganfalls könnte darin liegen, dass das POCD durch ein diffuses Embolisieren von Mikroembolien in Hirnareale, die weniger motorische als kognitive Funktionen repräsentieren, verursacht werden [Hogue 2008]. Somit sind die hier entwickelten Strategien zur Vermeidung von Schlaganfällen wahrscheinlich auch für die Vermeidung eines POCD relevant [siehe Kapitel 1.2].
Der Schlaganfall wird laut WHO als „akute neurologische Dysfunktion vaskulären Ursprungs mit plötzlichen oder raschem Auftreten von Symptomen und Zeichen, die mit umschriebenen Störungen der Gehirnareale korrespondieren“, definiert [WHO 1989]. Klassischerweise werden 3 Kategorien gemäß des zeitlichem Verlaufs der neurologischen Symptomatik unterschieden: *TIA* (Transient Ischemic Attack) mit vollständiger Rückbildung innerhalb von 24 Stunden, *RIND* (Reversible Ischemic Neurologic Deficit) mit Rückbildung innerhalb von 1-3 Wochen sowie *(Completed) Stroke* mit einer Persistenz der Symptomatik [A classification… 1975]. Früher ging man davon aus, dass nur beim (Completed) Stroke, manifeste Schädigungen der Hirnsubstanz vorliegen; durch neuere Untersuchungen mittels Diffusions-Gewichteter Magnetresonanztomographie (DW-MRT), weiß man mittlerweile,

dass auch bei TIAs in 30%-50% der Fälle ein ischämischer Hirninfarkte vorliegt. Folgende *neue Definition der TIA* wurde deshalb vorgeschlagen: „eine TIA ist eine vorübergehende Episode einer neurologischen Dysfunktion verursacht durch eine fokale Ischämie des Gehirns, des Rückenmarks oder der Retina ohne Hinweis auf einen akuten Infarkt“ [Easton 2009]. Als *neue erweiterte Definition des Schlaganfalls* wurde vorgeschlagen „ein Hirninfarkt ist ein Tod von Hirn- oder Retinazellen aufgrund einer prolongierten Ischämie“ [Saver 2008]. Unter diese Definition würden dann auch asymptomatische Hirninfarkte, welche sich beispielsweise als Zufallsbefund in der zerebralen Bildgebung zeigen, fallen. Solange nach dem Auftreten fokal neurologischer Symptome eine Unterscheidung in TIA oder Schlaganfall noch nicht möglich ist, wird in Anlehnung an das akute Koronarsyndrom nun empfohlen, von einem *akuten neuro-vaskulären Syndrom* zu sprechen [Easton 2009].

In den folgenden Arbeiten verwenden wir noch die klassische Unterteilung in *TIA, RIND* und *Completed Stroke*, weil diese als Ergebnisparameter in der von uns verwendeten Qualitätssicherung Herzchirurgie vorkommt, und als ein praktikabler Marker für die klinische Relevanz des postoperativen Schlaganfalls dient. Des Weiteren erscheint es uns sinnvoll, den perioperativen Schlaganfall in solche mit *früher*, d.h. unmittelbar mit dem Aufwachen aus der Narkose und solche mit *verzögert* auftretender Symptomatik einzuteilen; die intraoperativ entstandenen Hirninfarkte haben wahrscheinlich andere Risikofaktoren und Ursachen als solche, die bei Patienten entstanden sind, die zunächst unauffällig aus der Narkose erwachen und dann verzögert, in der ersten postoperativen Tagen einen Schlaganfall erleiden [Hogue 1999].

4.1.2. Ursachen

Die Schlaganfälle werden nach der, am ehesten wahrscheinlichen Ursache, in 4 bis 5 Gruppen eingeteilt. Klassischerweise geschieht dies nach klinischer Symptomatik und den Ergebnissen weiterführender Diagnostik. Die TOAST-Klassifikation unterscheidet [Adams 1993]: 1. Embolien aus Herz oder Aorta 2. Thrombose oder Embolie durch Atherosklerose einer größeren Hirnversorgenden Arterie, 3. Erkrankung der zerebralen Mikrovaskulatur, 4. Andere Ursachen wie globale Minderperfusion 5. Unbekannte Ursachen.

Der hohe Anteil der als unbekannt klassifizierten Ursachen gab Anlass, neue Klassifikationssysteme zu entwickeln: So bezieht das Causative Classification System (CCS) für die Zuordnung der Schlaganfälle zu den möglichen Ursachen auch die Risikofaktoren des Patienten mit ein, weil das Vorliegen bestimmter Risikofaktorenkonstellationen bestimmte

Schlaganfallursachen wahrscheinlicher machen [Ay 2005]; bei der A-S-C-O Klassifikation werden Wahrscheinlichkeitsränge für die jeweiligen möglichen Schlaganfallursachen gegeben, die auf der klinischer Symptomatik, weiterführender Diagnostik und Risikoprofil des Patienten fußen [Amarenco 2009]. Durch dieses heuristische Vorgehen lässt sich der Anteil, der als „unbekannte Ursache“ klassifizierten Fälle deutlich vermindern [Marnane 2010].

Eine typische Verteilung von Schlaganfall-Mechanismen in der Herzchirurgie zeigt Abbildung 1.

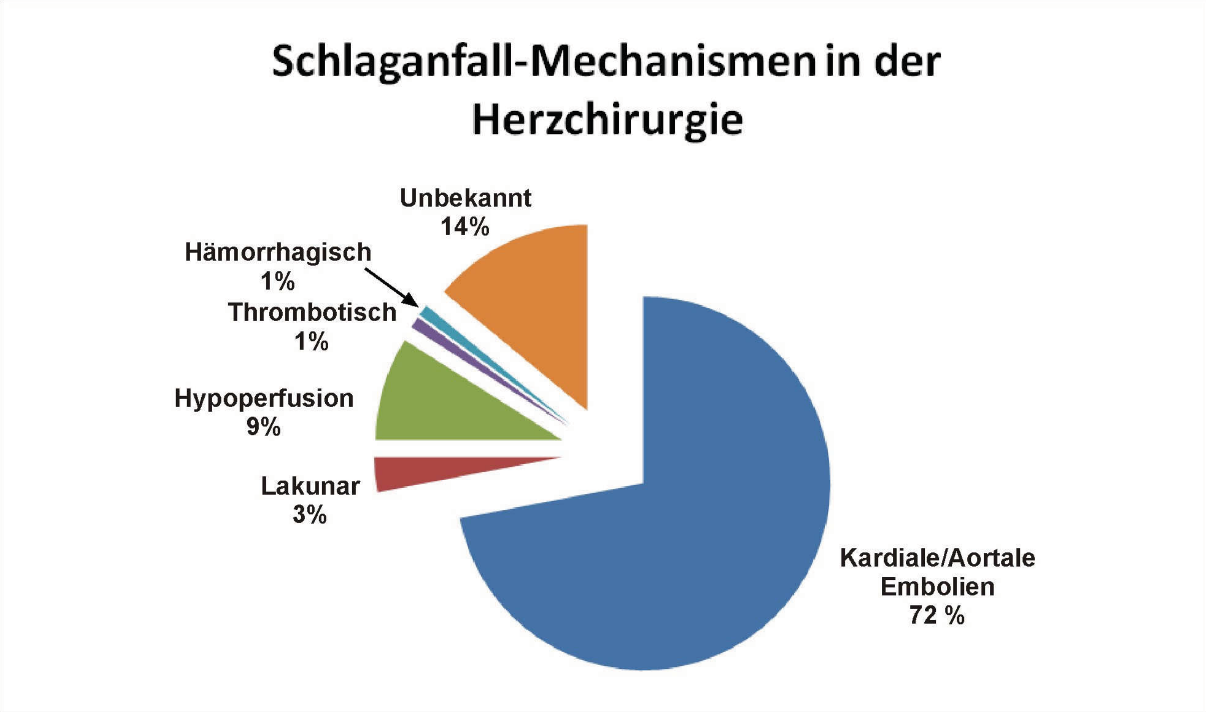


Abbildung 1. Verteilung der Schlaganfall-Mechanismen in der Herzchirurgie [Likosky 2003]

Schlaganfälle sind in der überwiegenden Zahl ischämisch bedingt, zerebrale Hämorrhagien sind mit einer Inzidenz von 1%-2%, je nach Operationsart, selten [McKhann 2006]. Die Hauptursachen von Hirninfarkten in der Herzchirurgie sind Embolien aus Herz oder Aorta sowie zerebrale Minderperfusion bei verminderter Pumpleistung des Herzens oder hypotone Phasen an der extrakorporalen Zirkulation [Hogue 2008].

Diese Risikofaktoren sind der Herzchirurgie inhärent und erklären die Tatsache, dass die Inzidenz von Hirninfarkten um ein Vielfaches höher ist als bei anderen Operationen (siehe Tabelle 1).

Eingriffsart	*Risiko (%)*	*Literatur*
Allgemeinchirurgie	0,08-0,7	[Kam 1997]
Koronare Bypassoperation	0,5-3,8	[Engelmann 1999, Roach 1996, Hogue 1999, Newman 1996, Likosky 2003, Sergeant 2004]
Koronare Bypassoperation & Aortenklappenersatz	3,4-7,4	[McKhann 2006, Hogue 1999, Barber 2008]
Aortenklappenersatz	1,2-5,0	[Bucerius 2003, Hogue 1999]
Zwei- & Dreifachklappenoperation	9,7	[Bucerius 2003]

Tabelle 1. Inzidenz des perioperativen Schlaganfalls. Modifiziert nach [Selim 2007].

4.1.2.1. Kardiale und aortale Embolien

Als Emboliequellen im Rahmen der Herzoperation kommen Embolien aus der thorakalen Aorta und aus dem Herzen selbst in Betracht (siehe Tabelle 2)

Der enge Zusammenhang zwischen Atherosklerose der Aorta und der Inzidenz zerebraler Komplikationen ist durch Autopsie-Studien und Risikofaktorenanalysen seit Langem bekannt [Djaiani 2006, Hogue 1999, Roach 1996,]. Eine Atherosklerose der thorakalen Aorta ist einerseits ein Marker einer generalisierten Atherosklerose, andererseits auch die Quelle zerebraler Embolien, welche durch intraoperative Manipulationen und Verletzungen der Aorta ausgelöst werden. So wurden bei Patienten mit atheromatösem Befall der Aorta ascendens vermehrt thrombotische Verschlüsse zerebraler Gefäße in Autopsie-Studien gefunden [Blauth 1992]. Studien mittels DW-MRT zeigten eine enge Korrelation des Schweregrads der Atheromatose der Aorta ascendens mit der Anzahl ischämischer zerebraler Läsionen [Djaiani 2004].

Emboliequelle	*Mechanismus*
Thorakale Aorta	
	I. Einführen und Entfernen der arteriellen Kanüle für die Herz-Lungen-Maschine in die distale Aorta ascendens II. Hochgeschwindigkeits-Strahl des aus der arteriellen Kanüle austretenden Blutes aus der Herz-Lungen-Maschine in den Aortenbogen (Sandstrahl-Effekt) III. Vertikale Klemmung der Aorta ascendens zum Ausschalten der Herzens aus der Perfusion IV. Anlage von aortokoronaren Venenbypässen in die mittlere Aorta ascendens a. Partielle Klemmung der Aorta ascendens b. Ohne Klemmung durch Anastomosen-Device (z.B. Heart String System oder Port)
Herz	
	I. Abschwemmen von Kalk oder resezierten Klappenanteilen bei Herzklappenoperationen II. Luft, welche sich in den Herzkammern oder den Lungenvenen ansammelt und nach Aortenklemmenöffnung in die zerebrale Zirkulation gelangt III. Luft aus der Herz-Lungen-Maschine IV. Ablösen von Vegetationen bei Endokarditis V. Lösen von Thromben im linken Vorhof oder Ventrikel

Tabelle 2. Mögliche Emboliequellen bei Herzoperationen.

Mit Hilfe des Transkraniellen Dopplers (TKD) konnte gezeigt werden, dass es bei allen Arten der Manipulation an der Aorta zu zerebralen Embolien kommen kann, wobei man im TKD immer noch nicht sicher zwischen gasförmigen und festen Partikeln unterschieden kann [Mackensen 2003, Schwarz 2011]. Plaque-Aufbrüche in der thorakalen Aorta, welche durch Kanülierungsmaßnahmen, Klemmungen oder den Sandstrahl-Effekt der aortalen Kanüle verursacht wurden, konnten im epiaortalen Ultraschall oder der Transösophagealen Echokardiographie dargestellt werden [Ura 2000, Swamanithan 2007]. Die Lokalisation des

atherosklerotischen Befalls im Bereich der distalen Aorta ascendens und der kleinen Kurvatur des Aortenbogens zeigt ein besonders hohes Schlaganfallrisiko an [Van der Linden 2007].
Bei der Koronaren Bypassoperationen sind Embolien dieser Art aus der thorakalen Aorta die einzig wesentliche Emboliequelle.
Bei Herzklappenoperationen besteht zusätzlich zum Risiko aortaler Embolien, das Risiko *(intra)kardialer* Embolien. In vielen Untersuchungen ergab sich daher eine höhere Schlaganfall-Inzidenz nach Herzklappenoperationen als nach Bypassoperationen (s.Tabelle 1).
Konsekutive Untersuchungen herzchirurgischer Patienten mittels DW-MRT zeigten in bis zu 45% aller Patienten neue ischämische zerebrale Läsionen, insbesondere im hinteren Stromgebiet [Leary 2007, Floyd 2006]. Studien, die versuchten die Anzahl der im DW-MRT gefundenen Läsionen oder der im TKD nachgewiesenen HITS mit der Inzidenz oder dem Ausmaß eines POCD zu korrelieren, kamen zu unterschiedlichen Ergebnissen [Hogue 2008, Barber 2008, Cook 2007, Knipp 2005]. Für die These, dass an der Ausbildung von POCD auch intraoperative Mikroembolien mitbeteiligt sind, sprechen Untersuchungen, die die Auswirkung von intraoperativen Maßnahmen zur Reduzierung gasförmiger oder partikulärer Mikroembolien untersuchten:

1) So führte die Verwendung eines speziellen Filters zum Abfangen gasförmiger Mikroembolien zu signifikant besseren neuropsychologischen Ergebnissen im Vergleich zur Kontrollgruppe ohne Filter [Gerriets 2010].
2) Mit Minimierung der intraoperativen Manipulation an der Aorta durch die sogenannte Single-Clamp-Technik sank nicht nur die Inzidenz von Schlaganfällen, sondern besserten sich auch die postoperativen kognitiven Leistungen [Hammon 2006].
3) Bei konservativer Behandlung der koronaren Herzkrankheit kam es seltener zum Auftreten eines POCD als nach Bypassoperation mit Herz-Lungen-Maschine [McKhann 2009].

Die aktuellen europäischen Richtlinien zur Myokardrevaskularisation nehmen dieses Problem der aortalen Embolien mit auf; es wird nun explizit empfohlen, während einer Bypassoperation die Manipulation an der Aorta zu begrenzen [Task Force on myocardial revaskularisation 2010]. Die wesentlichen Techniken, mit welchen sich eine Manipulation der Aorta minimieren oder gänzlich vermeiden lässt sind 1) eine durch epiaortalen Ultraschall geführte Kanülierung und Klemmung der Aorta, 2) die Vermeidung des partiellen

Ausklemmens der Aorta durch die Single-Clamp-Technik, 3) das Vermeiden der Herz-Lungen-Maschine (OPCAB) oder 4) das Vermeiden jeglicher Manipulation an der Aorta durch „Anaortic“ OPCAB. Metaanalysen prospektiv-randomisierter als auch retrospektiver Studien zeigen bereits eine signifikante Reduktion der Schlaganfallraten durch OPCAB [Kuss 2010]. Inwieweit eine weitere Reduktion durch die bisher kaum verbreitete „Anaortic OPCAB“ Technik möglich ist, bleibt noch unklar. Diesem Thema widmet sich die vorliegende Arbeit (Siehe insbesondere *Publikationen III-VI*). Bei dieser Technik erhalten alle Bypässe ihren Zufluss aus den Brustwandarterien, sodass in Kombination mit OPCAB keine Maßnahmen zur Bypassinsertion in die Aorta und damit überhaupt keine Manipulationen an der Aorta mehr notwendig sind.

4.1.2.2. Hypoperfusion & Embolie

Das gehäufte Auftreten von zerebralen Komplikationen nach Herzoperationen wurde neben dem hohen Risiko aortaler und kardialer Embolien vor allem auch mit der unphysiologischen Perfusion an der Herz-Lungen-Maschine in Verbindung gebracht. Hier spielt weniger der nicht-pulsatile Fluss als vielmehr die Gefahr globaler Hypoperfusion aufgrund von Hypotonien eine Rolle. So kam es in der vielfach zitierten Studie von Gold et al. bereits bei einem Blutdruckmittelwert an der EKZ von 50 bis 60 mmHg im Vergleich zu einem Mittelwert von 80mmHG bis 100 mmHg zu einer deutlich höheren Schlaganfallrate [Gold 1995]. Bei intakter zerebraler Autoregulation sollte ein Mitteldruck von 50 mmHg an der EKZ ausreichen. Insbesondere ältere Patienten sind aber aufgrund einer gestörten zerebralen Autoregulation, infolge eines langjährigen Hypertonus, zerebraler Gefäßerkrankungen oder Verlust der Elastizität der Gefäße, anfällig für Folgen von Hypotonien [Hogue 2006]. So führte in einer Studie mit älteren Patienten eine Reduktion des Blutdruckmittelwertes um 10 mmHg zum individuellen Ausgangswert zu einem 4.05 fachen Anstieg der Odds-ratio für einen bilateralen Grenzzoneninfarkt [Gottesman 2006]. Regionale Hypotonien an der EKZ entstehen insbesondere in der Aufwärmphase nach Hypothermie. So zeigten 27% bis 43% aller Patienten an der HLM pathologische zerebrale Sauerstoffsättigungen [Croughwell 1995]. Als Faustregel wird empfohlen, den Mitteldruck an der HLM entsprechend der Altersdekade zu halten: 50 mmHg für Patienten in der 5. Dekade, 60 mmHg für solche in der 6. Dekade und 70mmHg für Patienten in der 7. Dekade und aufwärts; so lässt sich die altersabhängige Störung der zerebralen Autoregulation kompensieren [Grogan 2008].

Regionale zerebrale Hypotonien an der HLM können auch durch eine ungünstige Ausrichtung des Strahls der aortalen Kanüle entstehen. Dieser Hochgeschwindigkeitsstrahl kann, wenn er an einer Öffnung eines supraaortalen Astes vorbeistrahlt, durch den Venturi-Effekt zu einer Minderperfusion dieses hirnversorgenden Gefäßes führen. Dies kann insbesondere bei Patienten mit Karotisstenose oder Verschluss ein zusätzliches Risiko für einen intraoperativen Hirninfarkt darstellen [Magilligan 1972, Kaufmann 2009].

In der Herzchirurgie besteht zusätzlich zum Risiko zerebraler Embolien, das Risiko von globalen Hypotonien bei Herz-Kreislaufversagen: so bei allen Zuständen, die mit einer verminderten Pumpleistung des Herzens einhergehen; beispielsweise bei akutem Myokardinfarkt, Kardiomyopathien im Stadium der Dekompensation, oder bei perioperativen Komplikationen wie Reanimation, Bypassinsuffizienz, Nachblutungen oder Perikardtamponaden. Auch ein schwerer Abfall des systemischen Gefäßwiderstandes im Rahmen eines SIRS oder einer Sepsis kann zu schweren Hypotonien und zerebraler Minderperfusion führen.

In der zerebralen Bildgebung ist ein Hirninfarkt, der aufgrund einer zerebralen globalen Minderperfusion aufgetreten ist, typischerweise in den Grenzzonen zwischen den Versorgungsgebieten der drei großen Hirnversorgenden Arterien lokalisiert. Dort, in den „letzten Wiesen" der Blutversorgung des Gehirns, führt eine globale Minderperfusion früher als in den anderen Regionen des Gehirns zu einer Unterschreitung der kritischen Durchblutungsschwelle und zur Ausbildung eines Hirninfarktes. Die Angaben über Häufigkeiten reiner Grenzzoneninfarkte schwanken in der Literatur sehr stark [Hogue 2008, Likosky 2003]. Der überwiegenden Zahl der Studien und auch unserer Erfahrung nach, sind reine Grenzzoneninfarkte selten.

Neben den durch Embolien ausgelösten „Territorialinfarkten" und den durch Hypoperfusion ausgelösten „Grenzzoneninfarkten" gibt es auch Mischbilder. Diese werden insbesondere bei Verwendung einer sensitiveren Diagnostik beispielsweise mittels DW-MRT häufiger diagnostiziert [Caplan 1998]. Hinter dieser häufiger in der Herzchirurgie beobachtbaren Kombination aus zerebraler Hypoperfusion und Embolie zeigt sich ein bislang minderbeachteter genereller Mechanismus der Schlaganfallgenese [Caplan 1998, Sedlaczek 2005]. Dieser Hypothese nach existiert ein natürlicher Mechanismus, der es ermöglicht, ischämische Schädigungen des Gehirns als Folge von Embolisationen in den Hirnkreislauf abzuwehren, nämlich den „washout of embolie". Durch diesen Mechanismus kann thrombogenes Material oder auch Luft, welches sich in den Hirnarterien festgesetzt hat, ausgeschwemmt werden. Kommt es jedoch zu einer globalen oder auch lokalen (z.B. hochgradige Karotisstenose) Minderperfusion, kann der Embolus nicht ausgewaschen werden, und der Embolus wird einen irreversiblen Gefäßverschluss verursachen, der einen Hirninfarkt zur Folge hat. Der „washout of embolie“ stellt somit eine pathogenetische Verbindung („link“) zwischen den Mechanismen Embolie und Hypoperfusion dar. Andere Beispiele aus dem klinischen Alltag, sind Schlaganfälle die durch Karotisstenosen ausgelöst werden: Während auch bei Karotis-Plaques oder wenig stenosierenden Karotisstenosen Embolien ständig nachweisbar sind, so steigt das Schlaganfallrisiko in dem Moment sprunghaft an, wenn die Karotisstenose hämodynamisch relevant wird und über eine regionale Minderperfusion zu einem gestörten „washout of embolie“ führt [Caplan 2006].

Diese Theorie ist für den klinischen Alltag in der Herzchirurgie wertvoll, weil sie die gleichzeitige Relevanz einer optimalen Hirnperfusion wie auch die Vermeidung kardialer oder aortaler Hirnembolien auf besondere Art verdeutlicht.

Bei 15% der Patienten, die OPCAB operiert wurden, stellte man einen Abfall der zerebralen Sauerstoffsättigung fest [Novitzky 2000]. Insbesondere während der Revaskularisierung der Hinter- und Seitenwand des Herzens kann es zu Hypotonien in Kombination mit Anstieg des zerebralen Venendrucks kommen. Für die OPCAB-Operation gilt daher im besonderen Maße, dass diese technisch in einer Art und Weise trainiert und ausgeführt werden muss, dass zerebrale Hypoperfusionen nicht vorkommen (*siehe Publikation IV*).

4.1.3. Risikofaktoren

Die Kenntnis von Risikofaktoren des perioperativen Schlaganfalls ist für die Aufklärung des Patienten, die mögliche Wahl einer alternativen Therapie und die Einleitung prophylaktischer Maßnahmen sinnvoll. Eine Reihe patientenbezogener Risikofaktoren wurden identifiziert: höheres Alter, weibliches Geschlecht und chronische Erkrankungen wie Hypertonie, Diabetes mellitus, Niereninsuffizienz, COPD, pAVK, koronare Herzerkrankung und Vorhofflimmern. Die mathematischen Modelle sind den Modellen zur Vorhersage der operativen Letalität (z.B. EuroSCORE) bezüglich ihrer Sensitivität und Spezifität vergleichbar; die Flächen unter der „Receiver Operating Characteristic-Kurve", die die Spezifität und Sensitivität der Vorhersagen wiedergibt, liegen dementsprechend bei 0.78-0.82 [Baker 2001, Bucerius 2003, Engelman 1999, Hogue 1999, Roach 1996, Newman 1996]. Die Studien, welche die Atherosklerose der Aorta ascendens als Variable mitberücksichtigten, fanden für die

Atheromatose der Aorta die höchsten Odds-ratios [Roach 1996, Hogue 1999]. Die Identifizierung folgender Risikofaktoren ist für die Prophylaxe von besonderer Bedeutung:

4.1.3.1. Karotisstenosen

Hochgradige Karotisstenosen sind eindeutig ein Risikofaktor für den perioperativen Schlaganfall [Baker 2001, Likosky 2003, Naylor 2011, Newman 1996]. Bei der Mehrzahl der Patienten die, bei Vorliegen einer hochgradigen Karotisstenose, perioperativ einen Schlaganfall erlitten, fand sich der Hirninfarkt kontralateral zur Seite der Karotisstenose oder im hinteren Stromgebiet, sodass in diesen Fällen eine durch die Karotisstenose bedingte ipsilaterale regionale Minderperfusion als Mechanismus des Schlaganfalls ausgeschlossen ist [Li 2010]. In einzelnen Fällen sind allerdings Grenzzoneninfarkte ipsilaterale zur Karotisstenose beobachtet worden und insbesondere bei Verschluss der A. karotis ist das Schlaganfallrisiko nochmals deutlich erhöht [Dashe 1997]. Es spricht einiges dafür, dass das Risiko für die Ausbildung eines ipsilateralen Hirninfarktes auch in der Herzchirurgie von der zerebrovaskulären Reservekapazität abhängen könnte. Eine eingeschränkte zerebrovaskuläre Reservekapazität ist ein Risikofaktor für einen ischämischen Hirninfarkt bei Patienten mit Karotisstenose oder Verschluss [Markus 2001, Silvestrini 2000]. Eine hochgradige, hämodynamisch wirksame Karotisstenose führt, wenn die Kollateralisierung über den circulus willisii nicht ausreichend ist, zu einem eingeschränkten Perfusionsdruck in den nachgeschalteten Hirnarealen, der durch eine Weitstellung der Gefäße bis zu einem gewissen Ausmaß kompensiert werden kann. Wenn die Weitstellung der Gefäße bereits an ihre Grenzen angekommen ist, wird eine globale Hypoperfusion, wie sie in der Herzchirurgie nicht immer zu vermeiden ist, zu einer Minderperfusion in den entsprechenden Hirnareale führen, und je nach Dauer und Ausmaß der Hypoperfusion zur Ausbildung eines Hirninfarktes führen. Präoperativ lässt sich durch Messungen des zerebralen Blutflusses in Ruhe und nach Gabe von Vasodilatatoren wie CO2, die zerebrovaskuläre Reservekapazität messen. Es ist daher folgerichtig, bei Vorliegen einer hochgradigen Karotisstenose mit eingeschränkter zerebrovaskulären Reservekapazität vor der Herzoperation eine Thrombendarteriektomie (TEA) oder ein Karotis-Stenting durchzuführen. Dies bedeutet, dass präoperativ alle Patienten auf das Vorliegen von Karotisstenosen untersucht werden müssen; wenn eine hochgradige Karotisstenose vorliegt, sollte die zerebrovaskuläre Reservekapazität überprüft werden. Je nach Dringlichkeit der kardialen Symptomatik kann dann eine Karotis-TEA im zeitlichen Abstand von mehreren Wochen vor der Operation oder simultan während der Herzoperation durchgeführt werden. Bei Karotisstenosen mit Indikation zur Karotis-TEA, welche jedoch eine gute zerebrovaskuläre Reservekapazität aufweisen, ist ein Eingriff mit zeitlichem Abstand von mehren Wochen nach der Herzoperation möglich.

4.1.3.2. Anamnese eines Schlaganfalls oder einer TIA

Schlaganfall oder TIA in der Anamnese sind unzweifelhaft Risikofaktoren für den perioperativen Schlaganfall [Baker 2001, Likosky 2004, Hogue 1999]. Das Risiko steigt, wenn das Ereignis kurz vor der Herzoperation stattgefunden hat. [Selim 2007]. Es wird empfohlen, nach einer TIA eine elektive Herzoperation für 3 bis 6 Monate auszusetzen [Selim 2007].

4.1.3.3. Notfalloperationen, schwere systolische Dysfunktion (EF<30%)

Bei Patienten die in hämodynamisch instabilem Zustand zur Herzoperation kommen und solchen, die eine schwer eingeschränkte Herzfunktion aufweisen, besteht, mehr als bei anderen Patienten, die Gefahr perioperativer Hypotonien. Diese Faktoren sind in vielen Untersuchungen als Risikofaktoren identifiziert worden [Selim 2007, Djaiani 2006, Hogue 1999]. Ein lückenloses perioperatives Monitoring der Hämodynamik und eine frühzeitige Therapie des Low Cardiac Output Syndrome sind wichtige prophylaktische Maßnahmen.

4.1.3.4. Hämatologische Faktoren

Hämatologische Faktoren, hätten gegenüber den oben beschriebenen Komorbiditäten, den Vorteil, kurzfristig modifizierbar zu sein. Wir führten daher eine systematische Untersuchung der wichtigsten Laborparameter durch; bisher waren diese in einem solchen Zusammenhang noch nicht untersucht worden (siehe *Publikation II*).

4.1.4. Qualitätsindikator

4.1.4.1. Qualitätssicherung & Klinik-Ranking

Der Parameter *„Seltenes Auftreten einer postoperativen zerebrovaskulären Komplikation“* stellt ein Qualitätsziel für die Bypasschirurgie in der externen Qualitätssicherung dar [www.sqg.de]. Die 95% *Referenzbereiche* für die Inzidenz postoperativ neu aufgetretenen Schlaganfälle lagen für die *Koronarchirurgie* 2009 bei ≤ 2.2% (Spannweite 0-4.8%), für die *Aortenklappenchirurgie* bei ≤ 3.0% (Spannweite 0-4,4%) und für die *Kombinierte Koronar- und Aortenklappenchirurgie* bei ≤ 4.7% (Spannweite 0-11,3%). Hat eine herzchirurgische

Klinik diese überschritten, wird der sogenannte *strukturierte Dialog* eingeleitet, in dessen Rahmen sich die betreffenden Kliniken für die schlechten Ergebnisse rechtfertigen müssen. Die Angaben der einzelnen Kliniken werden allerdings nicht systematisch überprüft.

4.1.4.2. Studien: Bypasschirurgie versus PTCA

Die Inzidenz der Schlaganfälle nach Bypassoperationen ist im Durchschnitt etwa zwei- bis dreifach so hoch wie nach PTCA [Bravata 2007]. Die Bedeutung dieses Endpunkts für die Indikation zur Bypassoperation wird in den aktuellen Diskussionen um die *Syntax-Studie* deutlich [Reichenspurner 2010, Schächinger 2010]. Diese prospektiv-randomisierte Multicenterstudie zeichnet sich durch die Verwendung moderner kardiologischer und herzchirurgischer Techniken wie ein hoher Anteil arterieller Bypässe oder Medikamenten-Beschichtete Stents sowie eine relativ hohe Rekrutierungsrate (70%) der Patienten, aus [Serruys 2009]. Diese Studie ergab nach 1, 2 und 3 Jahren eine hochsignifikante Überlegenheit der Bypassoperation bezüglich des kombinierten primären Endpunktes: „kardiale und zerebrovaskuläre Ereignisse (MACCE), einschließlich Mortalität und Notwendigkeit erneuter koronarer Revaskularisation nach einem Jahr. In den Analysen der einzelnen Endpunkte zeigte sich eine Schlaganfallrate nach Bypassoperation, die 4-Mal so hoch war, wie nach PTCA (2.2% versus 0.6%). Diese Studie ist für solche Aussagen zu Signifikanzunterschieden einzelner Komplikationen jenseits des primären oder der sekundären Endpunkte methodisch zwar nicht konzipiert, (z.B. bezüglich des „sample size"), dennoch sieht man in der höheren Schlaganfallrate der Bypassoperation ein relevantes Ergebnis und den bedeutendsten Nachteil der Bypassoperation gegenüber der PTCA [Schächinger 2010, From 2010]; weiterführende Studien zur Ausdehnung der Indikation zur PTCA beispielsweise auf Hauptstammstenosen berufen sich explizit auf dieses Ergebnis [http://clinicaltrials.gov/show/NCT01205789]. Insofern ist auch die Herzchirurgie aufgefordert, neue Wege zur Minimierung des Schlaganfallrisikos zu finden.

4.2. KLINISCHE DATENBANKEN

4.2.1. Entwicklung eines DataMart

Eine Voraussetzung für Risikofaktoranalyse des perioperativen Schlaganfalls sowie das Monitoring und die Bewertung neuer Operationstechniken ist eine an valider Information reichhaltige Datenbank [Kouchoukos 2003]. Für die Bewertung von Innovationen im Behandlungsablauf ist es auch von großer Bedeutung, historische Daten zu haben. Beispielsweise ist bei vollständiger Ablösung eines konventionellen durch ein innovatives Verfahren eine historische Kontrollgruppe notwendig, um den Innovationseffekt zu bewerten. Daher braucht man bereits für diese historische Kontrollgruppe eine prospektiv angelegte Datenbank, in der die perioperativen Patientendaten und die Nachbeobachtungsdaten systematisch erfasst werden [Treasure 2009].

In meiner Forschungsgruppe wurde eine spezielle klinische Datenbank entwickelt, ein DataMart, den wir aufgrund seines innovativen Konzeptes und des noch geringen Bekanntheitsgrades im Folgenden erläutern werden [Arnrich 2004a]:

In den allermeisten Kliniken liegt folgende Situation, die im Folgenden als konventionelle Datenbankarchitektur bezeichnet werden soll, vor: Während des gesamten Klinikaufenthaltes erheben verschiedene Fachabteilungen fallspezifische Daten mit teilweise unterschiedlichen Zielsetzungen. Diese Daten spiegeln Basis-, Prozess- und Ergebnisvariablen und sind häufig unerlässlich für aussagekräftige Untersuchungen klinischer Fragestellungen. Erfahrungsgemäß sind gerade herzchirurgische Datenbanken, die sich in der Vergangenheit in erster Linie auf Dokumentation, der für die externe Qualitätssicherung notwendigen Variablen, stützten, sowohl was Datenqualität („Eingabefehler“), Datenvollständigkeit („Missings“) und Datenvielfalt (wichtige Daten für Risikoscore fehlen) sehr mangelhaft geführt. Beispielsweise war es vor dem Jahr 2000 nicht möglich, den EuroSCORE, oder andere relevante Risikoscores, aus den Qualitätssicherungsdaten der Herzchirurgie nachzubilden.

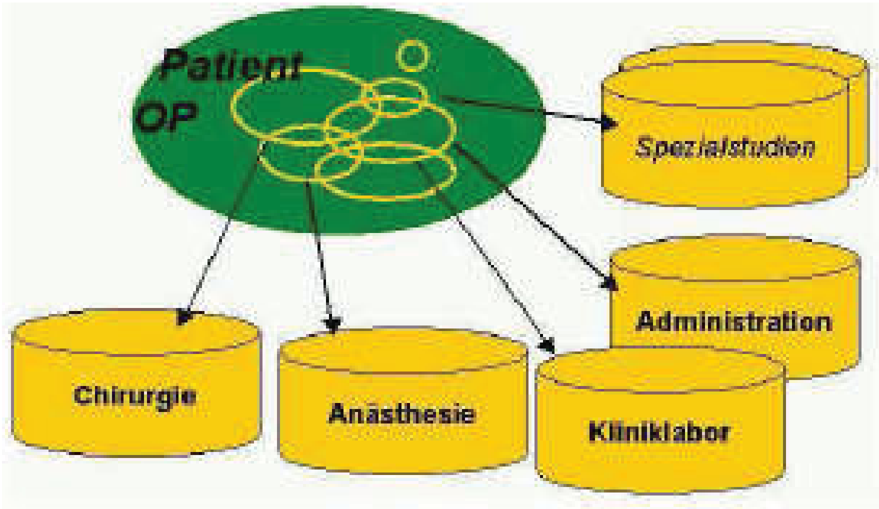


Abbildung 2: Patienten-spezifische Datenerfassung durch verschiedene Fachabteilungen

Um eine für die interne Qualitätssicherung (und wissenschaftliche Fragestellungen) brauchbare Datenbank zu erhalten, ist es in der Regel notwendig eine *Abteilungsübergreifende Datenbank* aufzubauen. Hier treten aber Probleme auf, weil in der Regel die Daten in getrennten klinischen Informationssystemen (KIS) von autonomen Abteilungen betrieben werden (die KIS unterstützen selten eine einfache Interprozesskommunikation), z.B. in folgender Struktur:

<u>Konventionelle Datenbank-Architektur</u>

CHIRURGISCHE Datenbank (Qualitätssicherung Herzchirurgie): medizinische Basis-, Therapie- und Verlaufsdaten;

ANÄSTHESIOLOGISCHE Datenbank: präoperative Anamnese und operativ-anästhesiologische Daten;

LABOR Datenbank

ADMINISTRATIVE Datenbank: Rechnungswesen und Verwaltung

ZUSÄTZLICHE Datensammlungen in vielfältigen Formaten stammen aus speziellen medizinischen Studien.

Bei der Zusammenführung der verschiedenen Datenbanken ergeben sich weitere Herausforderungen wie: Präferenz für Autonomie der Fachabteilungen, Minimierung des Arbeitsablaufrisikos und Schutz getätigter Investitionen (durch Haftpflichtregelungen und

Wartungsverträge sind Modifikationen an den bestehenden KIS ggf. sehr schwierig realisierbar), Einhaltung von Datenschutzbestimmungen, sowie die Integration der wertvollen Altdaten die eine Anpassung aller relevanten historischen Änderungen der Datenbankstrukturen in allen KIS (ausgelöst durch Software-Updates, Erweiterung der Erhebungsbögen, etc.) und den speziellen Datenformaten erfordert.

Als ausgesprochen effektiv hat sich eine in den letzten Jahren entwickelte DataMart-Architektur erwiesen.

Das *DataMart-System* spiegelt, extrahiert und konsolidiert alle relevanten Daten von den vorhandenen, unverbundenen KIS und den zusätzlichen Datensammlungen aus verschiedenen Spezialstudien. Damit konnten die zeit- und arbeitsaufwendigen Prozesse der Datensammlung und Konsolidierung ersetzt werden und eine stabile Forschungsdatenbank die reproduzierbare Ergebnisse ermöglicht, realisiert werden. Zurzeit enthält der DataMart auf der Intranet-Ebene 336 prä-, intra- und postoperative Attribute für über 25.000 Herzoperationen. Für Spezialfragestellungen sind weitere Daten auswertbar (>8 Millionen Laborwerte).

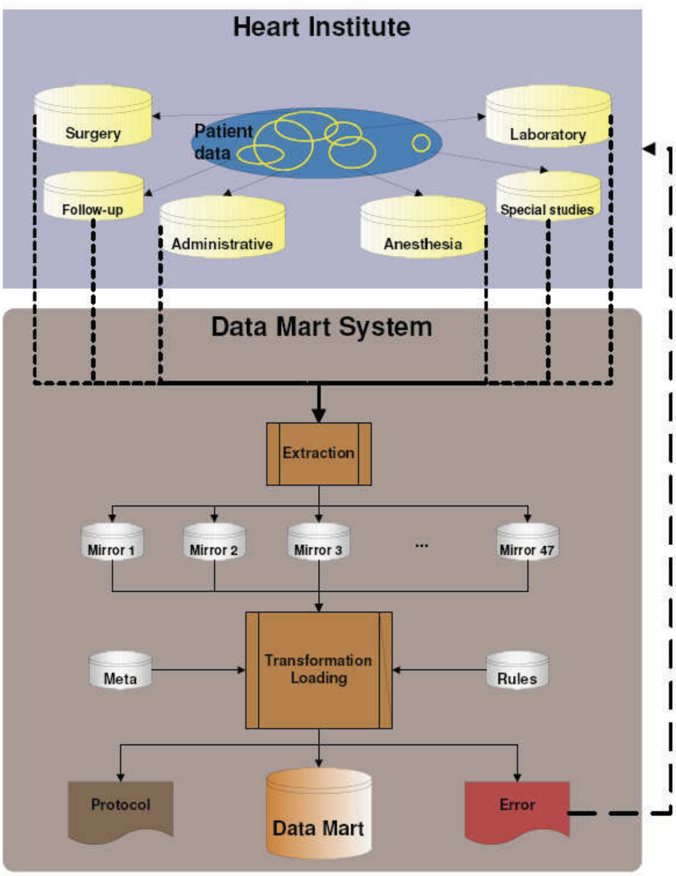


Abbildung 3: Aufbau des DataMart (aus Arnrich 2008)

Die Idee eines DataMart ist neu im Bereich der Herzchirurgie, deshalb haben wir die wichtigsten Kennzeichen dieses Systems in Tabelle 3 dargestellt:

DataWarehouse	*Register-Datenbank*	*DataMart*
Aggregierte Daten, zusammengefasst für Entscheidungsfindungsebene	Detailorientiert und fokussiert auf den einzelnen Patienten	Detailorientiert und aggregiert unter Einschluss von Routinedaten und Qualitätssicherungsdaten
Nur Lesezugriff	Lese- und Schreibzugriff	Lesezugriff, Veränderungen im KIS werden automatisch im DataMart umgesetzt
Periodisches Update durch Betriebssystem	Echtzeit Update durch Betriebssystem	Periodisches Update
Rohdaten häufig enthalten; Redundanz vorhanden	Aufgearbeitete (Normalisierte) Daten ohne Redundanz	Aufgearbeitete (Normalisierte) Daten mit Redundanz
Integriert Betriebs-, Klinik- und Finanzdaten	Integriert die üblichen klinische Daten	Integriert und konsolidiert alle forschungsrelevanten Daten und darüber hinaus
Speichert Daten mit Zeitmarken, Trendanalysen möglich	Speichert Daten in der neuesten Version	Speichert Daten in der neuesten Version, in tieferer Ebene aber Analysen von Daten mit Zeitmarken möglich
Daten werden automatisch eingespeist aus Betriebs-, Klinik- und Finanzsystemen	Daten werden aus Kliniksystemen eingespeist	Daten werden automatisch aus Betriebs- und Kliniksystemen, oder zusätzlich aus Nachbeobachtungstudien, lokalen Studien und Altdaten eingespeist

Tabelle 3: DataMart im Vergleich zum Datawarehouse und zur Register-Datenbank (in Anlehnung an Arnrich 2008)

4.2.2. Routinemäßige Nachkontrollen der Patienten

Externe Qualitätsvergleiche und internes Qualitätsmanagement stützen sich im Wesentlichen auf Daten, welche sich aus postoperativen Verlaufsbeobachtungen der Patienten nach Entlassung aus der primär versorgenden Klinik ergeben. Dementsprechend wird die Vollständigkeit der 30-Tage-Nachbeobachtungsrate von der BQS (bzw. AQUA) erwünscht, allerdings nicht verbindlich vorgeschrieben; so wiesen bis vor wenigen Jahren keine 15% der herzchirurgischen Abteilungen die geforderten Nachbeobachtungsraten von ≥97% auf,

Wir haben seit Jahren ein Modell der routinemäßigen Nachbeobachtung praktiziert [Albert 2004b]. Es ist mehrstufig aufgebaut und basiert zum Einen auf einer kontinuierlichen Dokumentation der wesentlichen anamnestischen und perioperativen Daten schon während des Krankenhausaufenthaltes im DataMart. Die reguläre Auswertung eingehender Arztbriefe der weiterbehandelnden Kliniken und Kardiologen im Rahmen des Tagesgeschäftes erlaubt eine Ergänzung des Datenbestandes ohne erheblichen Zusatzaufwand. Sechs Monate nach der Operation wird an alle Patienten ein rückfrankierter Fragebogen mit Fragen nach seinem gesundheitlichen und rehabilitativen Verlauf automatisch versendet. Dieser Fragebogen enthält auch die Fragen des „NHP". Der international anerkannten „Nottingham Health Profile" Fragebogen zur Lebensqualität enthält 38 subjektive Angaben zu Vitalität, Schmerzen, emotionaler Reaktion, Schlaf, sozialer Isolation und physischer Mobilität. Zur Vervollständigung der Statistik der 30 Tage und 6-Monats-Letalität werden in einer jährlich durchgeführten Aktion der Klinikärzte solche Patienten, deren Verlauf noch unklar blieb (ggf. auch deren Hausärzte), telefonisch kontaktiert.

Auswertungen zu diesen routinemäßig erhobenen prospektiven Daten zur 30-Tages–Letalität und zur Lebensqualität waren wesentliche Faktoren für das Verlassen der OPCAB-Methode Ende der 90er Jahre und Wiederaufnahme und Ausweitung des Verfahrens ab 2005 (siehe *Publikation VI*)

4.2.3. Monitoring und Bewertung

4.2.3.1. Externe und Interne Qualitätskontrollen

Die Befolgung von Leitlinien und Standards des diagnostischen und therapeutischen Prozedere garantieren noch keine optimale Behandlungsqualität. Eine Variabilität der Behandlungseffekte ergibt sich vor allem aus dem jeweiligen Können, der Erfahrung und der Motivation des Teams. Dabei ist das Können des Teams nicht allein die Summe der

Qualifikation aller Teammitglieder, sondern in eine komplexe soziale und psychologische Interaktion („Tacit Knowledge“) aller Beteiligten eingebettet [Pisano 2001]. Dies ist einer der Gründe, weshalb sich die unter Studienbedingungen erreichten Ergebnisse in breiter Anwendung nicht immer reproduzieren lassen und von Klinik zu Klinik Unterschiede in der Behandlungsqualität auftreten können.

Die externe Qualitätssicherung versucht nun die Behandlungsqualität einzelner Ärzte oder Kliniken zu messen. Die Ziele sind mitunter vielfältig: Sie reichen von bloßer Qualitätsdokumentation, über die Schaffung von Vergleichbarkeit (für Einweiser, Krankenkassen, Patienten und Angehörige) bis zur Ermöglichung eines transparenten Dienstleistungsmarktes. Nicht zuletzt wird durch breiteres Bewusstsein und Wettbewerb die Steigerung der Gesamtqualität angestrebt.

Die Erfahrungen reichen in den USA und England 20 Jahre zurück und zeigen wiederholt die Schwierigkeit des Unterfangens: Hauptprobleme sind

(i) eine unzureichende Berücksichtigung der Unterschiedlichkeit der einzelnen Patientenkollektive, d.h. ungenügende Risikoadjustierung und Risikomodellierung (z.B. EuroSCORE, siehe www.euroscore.org),

(ii) eine eingeschränkte Aussagekraft der verwendeten Qualitätsindikatoren;

(iii) die fehlende Kontrolle über die Richtigkeit der Angaben von Ärzten und Kliniken,

(iv) sowie die Unvollständigkeit der Falldokumentation insbesondere der Nachbeobachtungsdaten (siehe auch Qualitätsreports der BQS).

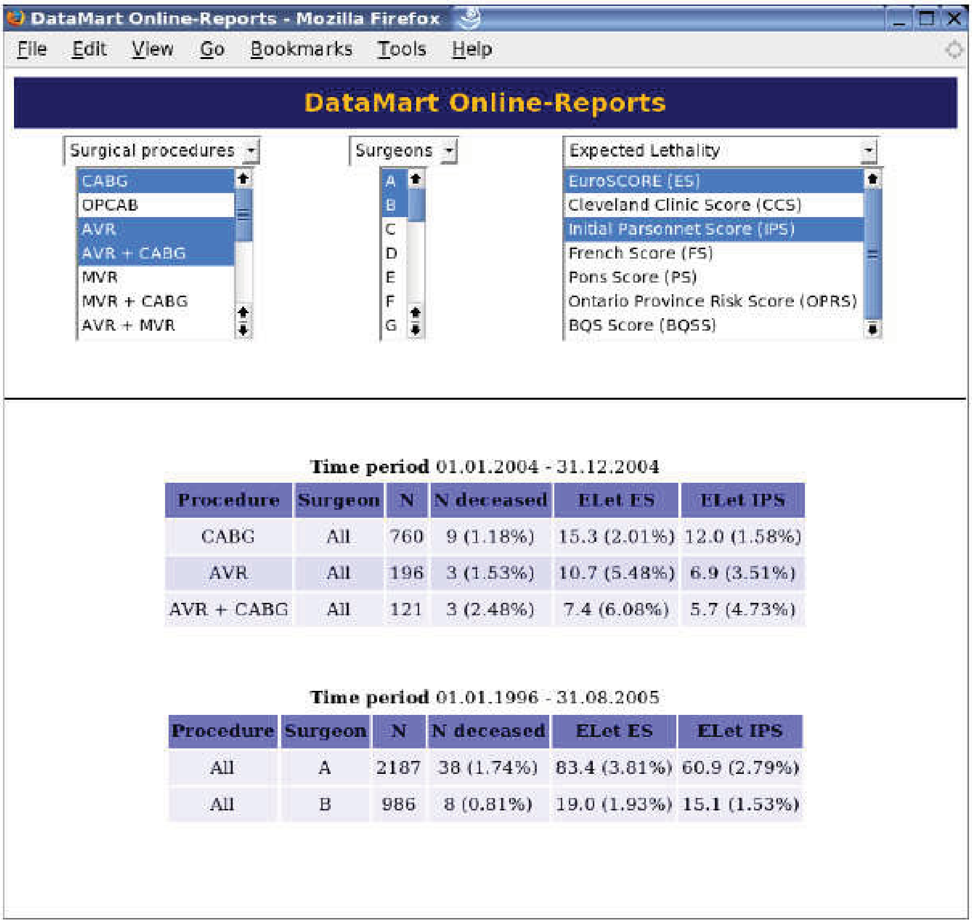
Demgegenüber hat die klinikinterne Kontrolle der Versorgungsqualität größere Möglichkeiten, medizinisch valide Aussagen zu den Behandlungsergebnissen zu treffen und Fehlverläufe zeitnah zu korrigieren. Dies setzt eine adäquate Datenbank sowie eine kontinuierliche Beobachtung, Reflexion und statistische Analyse der Behandlungsergebnisse voraus [Albert 2006].

Externe Qualitätskontrolle	*Interne Qualitätskontrolle*
Die Dokumentation ist auf wenige Kernvariablen beschränkt.	Breites Datenspektrum, der für die Bewertung des Krankheits- und Behandlungsverlaufs wesentliche Parameter verfügbar
Auswertungen und korrigierende Maßnahmen erfolgen in langen Zeitabständen zu den Ereignissen.	Behandlungsergebnisse können kontinuierlich erfasst und Fehlleistungen zeitnah korrigiert werden
Keine Kontrolle der Eingabequalität	Bessere Möglichkeiten zur Kontrolle der Eingabequalität
Nur wenige Kliniken mit vollständigem Follow-up	Die für die Bewertung spezieller Behandlungseffekte, Qualitätsindikatoren und Follow-up können ausgewertet werden.
Einfache Modelle zur Risikoadjustierung („EuroSCORE“)	Für die jeweilige Fragestellung spezifische Modelle werden ermittelt
Blackbox-Evaluation eines Qualitätsindikators ohne Einsicht in Ursache-Wirkungs-Beziehungen	Verfeinerte Analysen von Zeitmustern in den Daten können Aufschluss über die Folgen von Personal- oder Therapiewechsel geben

Tabelle 4: Externe im Vergleich zur Internen Qualitätskontrolle [nach Albert 2006]

4.2.3.2. Online-Berichtswesen

Ein wünschenswertes Ziel der internen Qualitätskontrolle ist es, möglichst zeitnah und transparent über Schwankungen der Performanz informiert zu werden. Eine Möglichkeit ist ein Intranet-basiertes Online-Berichtswesen; darauf können alle ärztlichen Mitarbeiter und im Forschungsbereich tätige Angestellte zugreifen und diverse aktuelle Statistiken zu Operationszahlen, Operationstypen und risikoadjustierten Letalitäten (je nach Zugangsberechtigung auch für Operateure) abfragen. Insbesondere die ärztliche Klinikleitung kann sich so besser einen Überblick über die Performanz der Abteilung erhalten.



Time period 01.01.2004 - 31.12.2004

Procedure	Surgeon	N	N deceased	ELet ES	ELet IPS
CABG	All	760	9 (1.18%)	15.3 (2.01%)	12.0 (1.58%)
AVR	All	196	3 (1.53%)	10.7 (5.48%)	6.9 (3.51%)
AVR + CABG	All	121	3 (2.48%)	7.4 (6.08%)	5.7 (4.73%)

Time period 01.01.1996 - 31.08.2005

Procedure	Surgeon	N	N deceased	ELet ES	ELet IPS
All	A	2187	38 (1.74%)	83.4 (3.81%)	60.9 (2.79%)
All	B	986	8 (0.81%)	19.0 (1.93%)	15.1 (1.53%)

Abbildung 4: Der Online-Report, eine Intranet-Applikation des DataMart

In dieser dargestellten Funktion des Online-Berichtswesens, kann der Anwender nach Operationsart (CABG, OPCAB, AVR, etc.), Chirurg (A, B, C, etc.), und/oder verschiedenen Risikoscores (EuroSCORE, Cleveland Clinic Score, etc) selektieren und die entsprechenden beobachteten mit den vorhergesagten Letalitäten vergleichen.

Eine weitere Funktion des Online-Berichtswesens sind Zeitliche Performanz-Darstellungen der Letalitäten, welche durch sogenannte *Variable Life Adjusted Displays (VLADs)* Kurven realisiert. Damit lassen sich im Gegensatz zu tabellarischen Auswertungen insbesondere temporale Kumulationen von Letalitäten zeitbezogen erkennen (siehe *Publikation 3).* Neben der Letalität können in ähnlicher Art und Weise zeitnah und risikoadjustiert andere Ergebnisparameter, wie beispielsweise die postoperative Dialysepflichtigkeit bewertet werden [Albert 2007].

Eine andere Möglichkeit ist das Monitoring zeitlicher Veränderungen mittels Daten-getriebener Dataminingverfahren, wie beispielsweise Assoziationsregeln, welche nach zeitlichen Veränderungen in den Datenbanken automatisch suchen, sodass weder die

Granularität der Zeit (Zeitintervalle), noch die Klassen vorgegeben werden müssen. Wir haben ein auf solchen Assoziationsregeln basierendes Verfahren weiterentwickelt, um zeitliche Irregularitäten in den Daten systematisch aufzuspüren und die optimalen zeitlichen Teilungspunkte statistisch zu verifizieren [Arnrich 2004b].

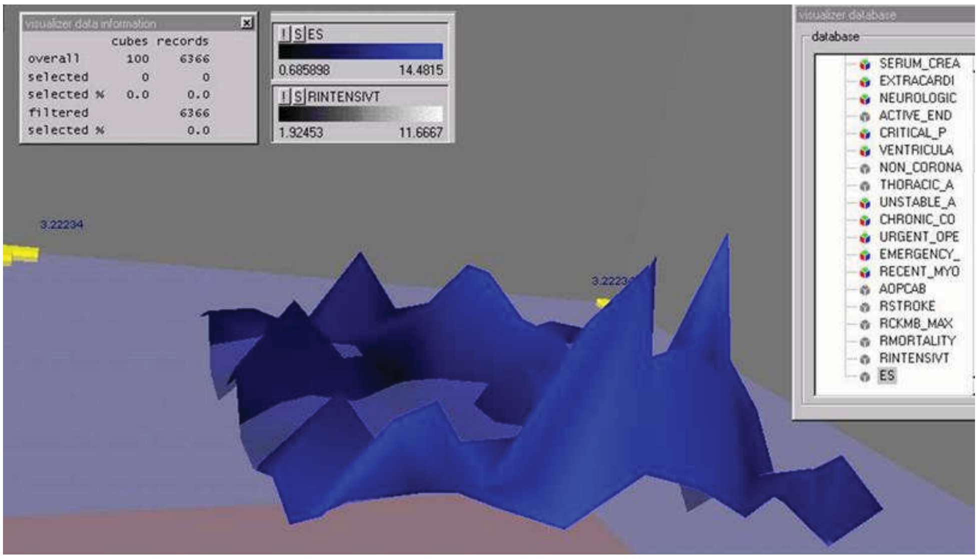
Um den Mitarbeitern Zugang zu den Daten über das Intranet zu erleichtern, wird eine automatisierte Exportfunktion zur Verfügung gestellt.

4.2.3.3 Datamining: Hypothesen-Bildung und Datenvisualisierung

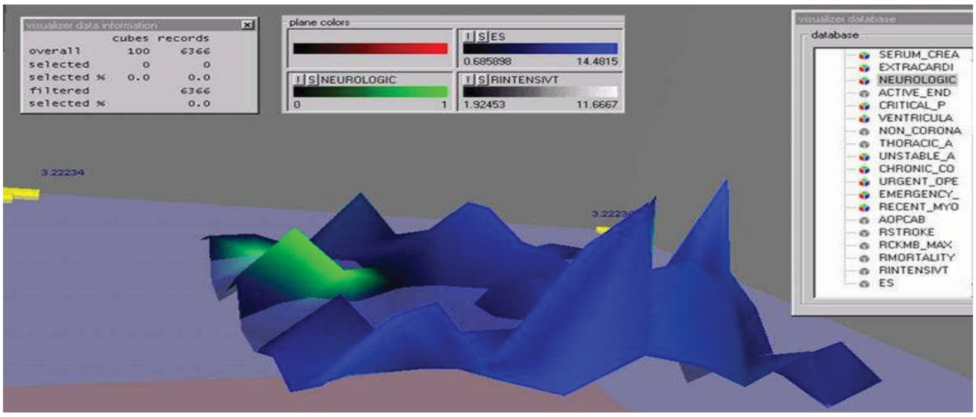
Bei hochselektiven Fragestellungen, wie die Identifikation von Einflussfaktoren auf den perioperativen Schlaganfall, schrumpfen die verfügbaren Fallzahlen, um statistisch robuste Aussagen treffen zu können; auch Trendabweichungen sind bezüglich ihrer potentiellen Zufälligkeit schwer zu beurteilen. Wir haben daher ein für die visuelle interaktive Anwendung durch den Arzt zugeschnittenes neuronales Netzwerk (SOM) auf herzchirurgische Daten angewendet [Albert 2002a]. Grundsätzlich kann eine visuelle Darstellung der Merkmalszusammenhänge für einen erfahrenen Spezialisten ein Mittel zur ausführlichen Diskussion der mitunter sehr vielschichtigen Zusammenhänge seiner Arbeit sein. Die räumliche Präsentation der Merkmale gibt Anlass, anders über die Zusammenhänge nachzudenken und deren komplexes Wechselspiel neu zu sehen. Sich darin bewegen zu können, ist Anreiz, interaktiv neue Ansichten zu erzeugen und mental zu verstehen, abzubilden und damit, in mehrfacher Hinsicht, zu visualisieren. In Abbildung 5 a-c sind über ein neuronales Netzwerk Merkmalszusammenhänge von 6366 Patienten visuell dargestellt; durch interaktive Arbeiten mit dem Programm wird hier die Hypothese gebildet, dass Patienten, die mit neurologischen Dysfunktionen eine Bypassoperation erhalten von OPCAB profitieren könnten.

Eine Möglichkeit, dieses Verhalten zu modellieren, ist die Verwendung von *Regressionsbäumen*, bei denen der Patientenbestand automatisiert in Subgruppen unterteilt und in jeder Partition ein Regressionsmodell berechnet wird; wir haben ein solches Verfahren zur automatisierten Suche von Hochrisikogruppen entwickelt, welches auf dem Prinzip beruht, dass die Datensätze baumartig in alle erdenkbaren Subgruppen aufgesplittert werden und die Schätzgenauigkeiten (z.B. Fläche unter der ROC-Kurve) optimiert werden (PRISMA) [Arnrich 2005].

a)



b)



c)

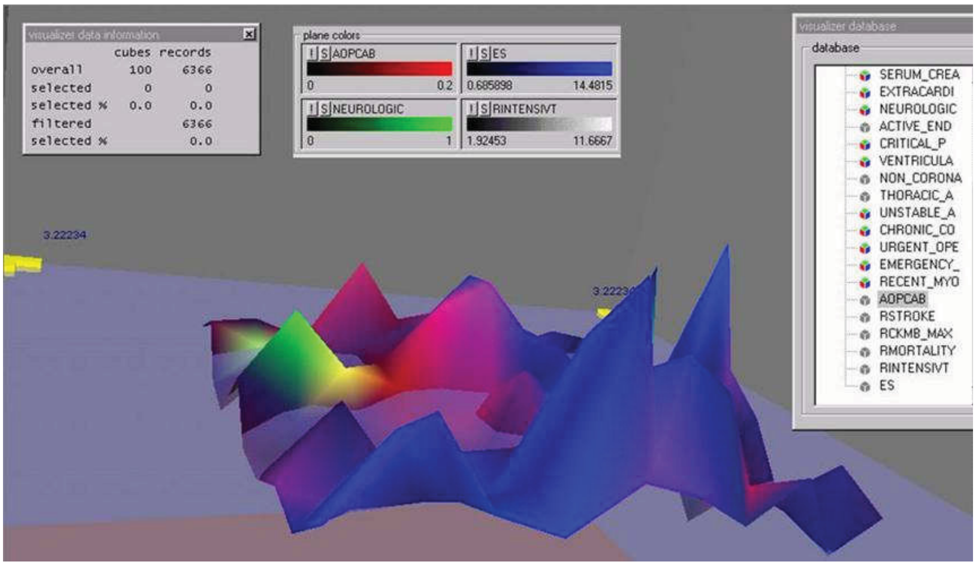


Abb. 5. Visualisierung des Zusammenhangs von OPCAB und Neurologischen Dysfunktionen (aus Albert 2002a)

Die Abbildung zeigt ein Beispiel einer SOM-Visualisierung zur Identifizierung einer

Erfolg versprechenden Behandlungsstrategie (OPCAB). Die Vertikalachse zeigt die Intensivaufenthaltsdauer (die verstellbare, graue Wasser-Fläche hilft den Höhenverlauf zu verdeutlichen), (ii) die Blauintensität der Flächenfärbung zeigt den mittleren Wert des EuroSCOREs, (iii) die Grünintensität zeigt die Häufigkeit präoperativer neurologischer Dysfunktionen und (iv) die Rotintensität zeigt den Anteil von OPCAB an den Bypassoperationen. Die Mischfarbe Hellgelb bedeutet hier, dass in diesem Bereich wenig Blau, aber viel Rot und Grün auf kleiner Höhe zusammentreffen. Sie ist benachbart zu einer Spitze gleichen Grüns (b), aber ohne Rotanteil (andernfalls Gelb). Das bedeutet, dass bei Vorliegen einer neurologischen Dysfunktion die OPCAB-Technologie im Mittel zu kürzeren Aufenthalten in der Intensivstation führt.

5. EIGENE ARBEITEN

Fragestellungen

1) Einer gängigen Hypothese zu Folge, ist der Sandstrahl-Effekt des aus der Aortenkanüle auf die Aortenwand schießenden Blutes ein wichtiger Risikofaktor des herzchirurgischen Schlaganfalls. Uns interessierte, ob die Form der Spitze der aortalen Kanüle, die die Geschwindigkeit und Richtung des Blutstromes mitbestimmt, Einflüsse auf die Lokalisation und Inzidenz des Schlaganfalls hat.

2) Um die Interaktion zwischen patienteneigenen und chirurgischen Risikofaktoren für das Auftreten von postoperativen Schlaganfällen besser zu verstehen und um vermeidbare Risikofaktoren zu identifizieren, führten wir eine Studie auf der Basis des DataMarts durch, welche alle im Zeitraum von 1997 bis 2000 operierten Patienten einschloss. Erstmals wurden auch alle gängigen Routinelaborwerte in eine Risikofaktorenanalyse mit aufgenommen, um festzustellen, ob sich hierunter vermeidbare Risikofaktoren befinden.

3) Über die oben genannten Strategien der Risikovermeidung durch adäquate OP-Vorbereitung und intraoperative Modifikation der Techniken der extrakorporalen Zirkulation hinaus, kann durch das OPCAB-Verfahren die Manipulation an der Aorta minimiert und der Sandstrahl-Effekt vermieden werden. Da dieses Verfahren jedoch technisch anspruchsvoll ist und bei unsachgemäßer Anwendung mit einem Risiko für den Patienten einhergeht, benötigt man spezielle Methoden zur Überwachung der Ergebnisqualität. Hier entwickelten wir ein auf dem DataMart basierendes Kontrollverfahren, um frühzeitig festzustellen, ob es durch die neue Methode zu Abweichungen der Behandlungsqualität gegenüber dem Standardverfahren kommt.

4) Nachdem das OPCAB-Verfahren aufgrund der unzureichenden Ergebnisse zunächst verlassen worden war, sollte es unter besseren Voraussetzungen wieder eingeführt werden. Zunächst wurde das Verfahren durch den Autor während eines einjährigen externen Aufenthaltes neu trainiert und es wurden neue Trainingskonzepte entwickelt. In einer Untersuchung an 50 herzchirurgischen Teams, die einen zweitägigen Trainingskurs an der Universität Leuven/Belgien besuchten, sollte festgestellt werden, welche Faktoren für eine erfolgreiche Etablierung des Verfahrens von Bedeutung sind.

5) Um die Standardisierung und damit die Reproduzierbarkeit und Ausbreitung von der anaortic OPCAB-Operation zu fördern, entwickelten wir eine Formel zur Abschätzung der erforderlichen Bypasslänge für eine Revaskularisation mit beiden Brustwandarterien. An 100 konsekutiven Operationen prüften wir, ob diese Formel reproduzierbar die erforderliche Bypasslänge voraussagt.

6) Nachdem das OPCAB-Verfahren Eingang in die tägliche Routine aller Chirurgen der Abteilung gefunden hat, wurde die Entwicklung von der konventionellen Bypasschirurgie bis zur nahezu kompletten Umstellung auf TOPCAB analysiert und die Methode bewertet. Ein besonderer Schwerpunkt lag auf der Frage, ob durch die Umstellung auf TOPCAB das erklärte Ziel einer signifikanten Reduktion neurologischer Komplikationen erreicht wurde.

5.3.1. Hat die Form der Aortenkanüle einen Einfluss auf den postoperativen Schlaganfall? Klinische Beurteilung gerader und gebogener Aortenkanülen (Originalpublikation I)

Albert A, Beller C, Arnrich B, Walter J, Rosendahl U, Hetzel A, Priss H, Ennker J (2002). Is there any impact of the type of aortic end-hole cannula on stroke occurrence? Clinical evaluation of straight and bent-tip aortic cannulae. *Perfusion 17*: 451-456.

Bei athero-thrombotisch veränderten Aorten besteht die Gefahr, dass sich durch externe chirurgische Manipulation oder den Sandstrahl-Effekt, des aus der Aortenkanüle auf die gegenüberliegende Aortenwand schießende Bluts, Plaques aufbrechen können; dadurch kann sich atheromatöses Material ablösen, in den Hirnkreislauf gelangen, und Gefäßverschlüsse verursachen. Ein weiteres Risiko, dass mit dem arteriellen Zufluss aus der Herz-Lungen-Maschine in die distale Aorta ascendens assoziiert ist, besteht darin, dass ein aus der Kanüle austretender Hochgeschwindigkeits-Strahl, durch Unterdruck-Effekte, zu einer Minderperfusion supraaortaler Äste, führen kann [s. Kapitel 1.2.].

Anlass zur folgenden Untersuchung war ein kurz zuvor publizierter Bericht, der erstmals über eine Seitendominanz postoperativer Hirninfarkte berichtete. Der Autor hatte deutlich mehr Hirninfarkte auf der linken als auf der rechten Hemisphäre seiner Patienten beobachtet und führte das auf die Verwendung gebogener Aortenkanülen zurück. Er vermutete, dass die gebogenen Kanülen den Blut-Ausstrom gegen den Abgang der linken A. karotis leiteten und dort durch den Sandstrahl-Effekt athero-thrombotisches Material ablösen könnten. Die Aussagekraft dieser Studie war insofern beschränkt, weil hier kein Vergleichskollektiv vorhanden war; alle Operationen waren mit gebogenen Kanülen durchgeführt worden. In unserer Klinik wurden sowohl gerade als auch gebogene Aortenkanülen verwendet, sodass wir in der Lage waren, die von dem Autor geäußerte Hypothese zu testen.

An einem Kollektiv 8129 am Herzen operierter Patienten untersuchten wir, welchen Effekt die Form der Spitze der Aortenkanüle, auf die Lokalisation, die Inzidenz und den klinischen Schweregrad der postoperativen Schlaganfälle haben könnte. Im multivariaten Model wurden auch andere Faktoren, die möglicherweise die Lokalisation der Hirninfarkte beeinflussen konnten, wie unilateralen Karotisstenosen, mitberücksichtigt.

Wir konnten die Hypothese, dass gebogene Aortenkanülen mit linkshemisphärischen Hirninfarkten korreliert seien, nicht bestätigen. Dagegen kam es bei Verwendung gerader Aortenkanülen signifikant häufiger zu bilateralen oder posterioren Infarkten. Zudem korrelierte die Verwendung gerader Aortenkanülen mit einer höheren Inzidenz und Schweregrad der Schlaganfälle.

Dies Ergebnis erklärt sich am ehesten durch die unterschiedliche Orientierung der Kanülenspitze in der Aorta. Im Falle der geraden Kanüle, welche damals üblicherweise vertikal zur distalen Aorta ascendens inseriert wurden, schießt der Blutstrom wegen der kurzen Distanz mit großer Geschwindigkeit auf die posteriore Wand der Aorta unterhalb aller supraaortalen Äste; im Falle gebogener Kanülen wird der Blutstrom parallel zum Verlauf des Aortenbogens gelenkt und trifft, bei exakter Ausrichtung, erst nach Abgang der supraaortalen Äste und nach deutlichem Verlust an kinetischer Energie die Aortenwand.

Dies bedeutete für die tägliche Praxis, dass nunmehr gleich welche Kanülenform verwendet wird, die Kanülenöffnung immer parallel zum Aortenbogen ausgerichtet wird. Dies ist bei weit distaler und leicht schräger Aorten-Insertion, wegen des nach posteriore verlaufenden Aortenbogens, auch bei der geraden Kanüle möglich. Die Bedeutung des Venturi-Effekts ist ebenfalls von der Position der Kanüle abhängig, wie jüngere Untersuchungen zeigen [Kaufmann 2009].

Is there any impact of the shape of aortic end-hole cannula on stroke occurrence? Clinical evaluation of straight and bent-tip aortic cannulae

AA Albert[1], CJ Beller[1], B Arnrich[2], JA Walter[2], UP Rosendahl[1], A Hetzel[3], H Priss[4] and J Ennker[1]

[1]*Department of Cardiothoracic Surgery, Heart Institute Lahr/Baden, Lahr, Baden-Württemberg, Germany;*
[2]*Institute of Neuroinformatics, University of Bielefeld, Bielefeld, Germany;*
[3]*Department of Neurology, University of Freiburg, Freiburg, Germany;*
[4]*Department of Neurology, Clinic Lahr, Lahr, Germany*

Objective: To compare the impact of straight and bent-tip aortic cannulae on stroke occurrence, location, and severity. Methods: Prospective data were collected on 8129 patients (coronary artery bypass grafting (CABG) and/or valvular surgery). 'Bent-tip' aortic cannulae were used in 15.6% of cases and 'straight' end-hole cannulae in 84.4% of cases. Results: There were a total of 137 strokes: right anterior 52, left anterior 39, bilateral 23, posterior 18, and location not established 5. With the use of bent-tip cannulae, the incidence of strokes was 0.9% versus 1.8% with straight cannulae (χ^2, $p=0.026$). Bilateral and posterior strokes occurred more often with the use of straight cannulae (χ^2, $p=0.015$). Straight cannulae also related to the severity of strokes (χ^2, $p=0.003$). Conclusions: There is an influence of the type of cannula on the occurrence, location, and severity of strokes. Straight cannulae cause significantly more often and more severe bilateral and posterior strokes than bent-tip cannulae. *Perfusion* (2002) **17,** 451–456.

Introduction

The incidence of neurological disorders after cardiac surgery remains high despite different efforts aimed at reducing neurological injury.[1] Several risk factors for the incidence of stroke after cardiac surgery have been identified.[1–3] Atheroembolism from the aorta, especially originating from the ascending and the arch areas, is one of the major causes of stroke after cardiac surgery.[4–6] External manipulation of the aorta and the 'sand blasting' effect of the high-velocity jet passing the aortic cannula can cause dislodgment of atheromatous debris.[5,6] A correlation between bent-tip aortic cannula and left hemispheric territorial infarction was recently established.[7]

The purpose of this study is to investigate the possible influence of straight versus bent-tip aortic cannulae on the occurrence, severity, and location of stroke, which may occur during or after cardiac surgery.

Address for correspondence: Alexander A. Albert, MD, Hohbergweg 2, Lahr 77933, Germany.
E-mail: alexander.albert@heart-lahr.com

Materials and methods

From March 1996 to December 2000, 8744 adult patients underwent cardiac surgery at the Heart Institute Lahr/Baden. Patients with surgery on the thoracic aorta, those with 'off-pump' coronary artery bypass grafting (CABG), and patients who underwent simultaneous carotid endarterectomy were excluded. This left 8129 cases in the study; of these, 5979 underwent CABG. Six hundred and sixteen had simultaneous valvular procedures, 689 had isolated aortic valve replacements, 206 had isolated mitral valve replacements, and 60 had double valve replacements. In 81, the valve – and in 274, CABG – was a 're-do'. One hundred and ten patients had 'other' major cardiac surgical procedures. Data of quality assessment were collected prospectively on all patients using the standardized protocols of the German Society of Thoracic and Cardiovascular Surgery and the German Society of Anaesthesiology and Intensive Care Medicine.[8,9] Additional variables, including, for instance, data concerning the operating team, degree of carotid stenosis if present, and the degree of aortic

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atherosclerosis and history of neurological disease, were recorded. The data were stored perioperatively in three commercially available electronic databases (Medwork, Datapec, Clinicom, Düsseldorf, Germany), consolidated, and transmitted to a 'Data-mart' system. For the present study, we analysed 33 out of more than 160 attributes collected for each patient.

Clinical preoperative studies included Doppler ultrasonography and spirometry of the carotid and the vertebral arteries. A neurological consultation was obtained in patients with high-grade carotid stenosis and/or history of neurological disorders to assess existing preoperative neurological deficits and to facilitate a distinction from possible perioperative neurological events.

Assessment of aortic calcification was obtained by intraoperative palpation and by visualization, starting in 1998 (3245 cases were analyzed). Postoperatively, all patients were evaluated for possible neurological deficits. In cases where either focal neurological deficits or prolonged loss of consciousness were detected, neurological consultation was obtained. Depending on the severity of symptoms, CT scan of the brain was performed and interpreted independently by the radiologist and the neurologist. Patients with established brain injury following resuscitation from cardiac arrest were excluded from the study. Residual neurological deficits were registered four to six weeks after discharge. In the course of clinical data analysis, a systematic chart review was done in 137 patients who suffered a stroke.

Classification of strokes

Clinical manifestations of cerebrovascular accidents (CVAs) were classified as 'transient ischaemic attack' (TIA), 'prolonged reversible ischaemic neurological deficit' (PRIND), or 'completed' stroke (CS). Patients with pre-existing neurological deficits who developed new neurological symptoms or obvious prolonged worsening of already existing symptoms were diagnosed as having a 'new' stroke.

The location of the stroke was established by CT and/or clinical syndromes as 'left' or 'right anterior' (territory of the left or right carotid artery), or 'posterior' (territory of the vertebrobasilar system). In cases where the infarction involved or extended into both vascular territories, it was classified according to the affected carotid artery as 'right anterior' or 'left anterior'. This classification was applied to 'borderline' infarctions, which are known often to be caused by embolic events.[10] In cases of posterior infarcts, we did not attribute a specific pathway to the passage of embolic material.

Perioperative management

The patients were operated on by 12 different surgeons. At the completion of the median sternotomy, heparin (375 kIU/kg) was given to obtain an activated clotting time in excess of 400 s. The ascending aorta was cannulated for cardiopulmonary bypass in a spot free of atherosclerotic plaque. Bent-tip aortic cannulae were used in 15.6% (Medos 6.5 mm: Medizintechnik, Stollwerk, Germany) and straight end-hole cannulae in 84.4% of all cases (Medos 8.0 mm: Medizintechnik; Jostra 8.0 mm reinforced with ring: Medizintechnik, Hierlingen, Germany) (Table 1). According to surgeon's preference, bent-tip or straight cannulae were chosen. Jostra HL 20 heart–lung machines with capillary oxygenators were used. Roller pumps were applied to generate nonpulsatile flow. Target CPB flow was between 90% and 120% of the calculated value (body surface area multiplied by 2.5). When mild hypothermia (down to 32°C) was used, the systemic flow was decreased to 2.0 l/min/m^2 (dependent on venous oxygen saturation). Beginning in 1998, patients were kept normothermic (> 35°C) during most CABG. Alpha-stat blood gas management was used. The 'target' perfusion pressure was 60 mmHg, and 60–80 mmHg for patients with known carotid stenoses. The perfusion pressure was maintained with noradrenalin wherever it was necessary. Patients who were still with low cardiac output or who needed adrenalin >0.2 μg/kg/min after being weaned off cardiopulmonary bypass were placed on intra-aortic balloon pump (IABP).

Statistical analysis

Univariate comparisons between subjects with and without CVA were performed with chi-square tests for categorical data. Spearman's rank order and Kendall's tau-b test were carried out for ordinal data. Statistical tests were analysed by SPSS (version 8.0).

Results

Characteristics of patients with strokes

The prevalence of stroke was 1.7% (n=137). Stroke rate was 0.9% (n=12) with the use of bent-tip cannulae, and 1.8% (n=125) with the use of straight cannulae. Fifty-one per cent of stroke patients had an alteration of vigilance (n=70). In-hospital mortality rate of stroke patients was 10.2% (n=14) versus 2.5% of patients without stroke (n=200). CT scans of

Table 1 Characteristics of cannulae

Cannula type		*Outer diameter (mm)*	*Pressure gradient*[a] *(mmHg)*
Jostra	Straight	8.0	23
Medos	Straight	8.0	14
Medos	Bent-tip	6.5	60

[a]At a flow rate of 5 l/min water.

Table 2 Pre-, intra-, and postoperative variables assessed as univariate predictors of stroke

Variables	*No CVA,* n *(%)*	*CVA,* n *(%)*	p *value*	*Odds ratio*
IABP	87 (1.1%)	7 (5.1%)	< 0.001	4.64
Aortic calcification	120 (3.6%)	9 (14.3%)	< 0.001	3.97
History of stroke	628 (7.9%)	31 (22.6%)	< 0.001	2.86
Carotid stenosis	801 (10.0%)	38 (27.7%)	< 0.001	2.77
Preoperative atrial fibrillation	527 (6.6%)	25 (18.2%)	< 0.001	2.76
CNS disease	496 (6.2%)	21 (15.3%)	< 0.001	2.47
Peripheral vascular disease	825 (10.3%)	27 (19.7%)	< 0.001	1.91
Age (years)			< 0.001	
< 60	1989 (24.9%)	9 (6.6%)		0.27
60–70	3080 (38.5%)	51 (37.2%)		0.97
>70	2923 (36.6%)	77 (56.2%)		1.54
Postoperative atrial fibrillation	3793 (47.5%)	91 (66.4)	< 0.001	1.40
General condition			< 0.001	
Normal	2327 (29.1%)	28 (20.4%)		0.70
Reduced	4829 (60.4%)	82 (59.9%)		1.0
Severely reduced	836 (10.5%)	27 (19.7%)		1.88
Diabetes mellitus	2120 (26.5%)	52 (38.0%)	0.003	1.43
COPD	1538 (19.2%)	39 (28.5%)	0.007	1.48
Ejection fraction (%)			0.007	
< 30	498 (6.2%)	13 (9.5%)		1.53
30–55	2462 (30.8%)	54 (39.4%)		1.28
>55	5032 (63.0%)	70 (51.1%)		0.81
NYHA class			0.009	
I	1460 (18.3%)	26 (19.0%)		1.04
II	2593 (32.4%)	24 (17.5%)		0.54
III	3422 (42.8%)	70 (51.1%)		1.19
IV	517 (6.5%)	17 (12.4%)		1.9
Operating time (min)			0.02	
< 180	2226 (27.9%)	28 (20.4%)		0.73
180–240	3927 (49.1%)	68 (49.6%)		1.01
>240	1840 (23.0%)	41 (29.9%)		1.3
Straight aortic cannula	6737 (84.3%)	125 (91.2%)	0.026	1.1
Total CPB time (min)			0.03	
< 90	3942 (49.3%)	54 (39.4%)		0.80
90–120	2501 (31.3%)	51 (37.2%)		1.19
>120	1549 (19.4%)	32 (23.4%)		1.21
Hypertension	5446 (68.1%)	105 (76.6%)	0.034	1.12
Operation			0.038	
Elective	6168 (77.2%)	94 (68.6%)		0.89
Urgent	1287 (16.1%)	31 (22.6%)		1.40
Emergent	537 (6.7%)	12 (8.8%)		1.31
Mitral stenosis	121 (1.5%)	5 (3.6%)	0.045	2.4
Female sex	2348 (29.4%)	51 (37.2%)	0.046	1.3
Nonsignificant variables				
Temperature during CPB (°C)			0.069	
33–37	5458 (68.3%)	83 (60.6%)		0.89
30–33	2367 (29.6%)	50 (36.5%)		1.23
25–33	140 (1.8%)	3 (2.2%)		1.22
< 25	27 (0.3%)	1 (0.7%)		2.33
Body mass index (kg/cm^2)			0.096	
< 20	155 (1.9%)	4 (2.9%)		1.53
20–25	2157 (27.0%)	45 (32.8%)		1.21
>25	5680 (71.1%)	88 (64.2%)		0.90
Previous cardiac surgery	394 (4.9%)	11 (8.0%)	0.098	1.63
Aortic valve disease	1655 (20.7%)	36 (26.3%)	0.111	1.27
Pulmonary hypertension	382 (4.8%)	10 (7.3%)	0.172	1.52
Mitral insufficiency	409 (5.1%)	10 (7.3%)	0.252	1.1
Aortic cross-clamp time (min)			0.415	
< 60	4679 (58.5%)	76 (55.5%)		0.95
60–120	3238 (40.5%)	58 (42.3%)		1.04
>120	75 (0.9%)	3 (2.2%)		2.44
Aortic stenosis	1111 (13.9%)	22 (16.1%)	0.47	1.16
Intraoperative ultrafiltration	120 (1.5%)	3 (2.2%)	0.513	1.5
Aortic insufficiency	714 (8.9%)	11 (8.0%)	0.713	0.9
Left main stenosis	1350 (16.9%)	22 (16.1%)	0.796	1.0
LV aneurysmectomy	127 (1.6%)	2 (1.5%)	0.904	0.94

CVA: cerebrovascular accident; CPB: cardiopulmonary bypass; LV: left ventricle; CNS: central nervous system; COPD: chronic obstructive pulmonary disease; NYHA: New York Heart Association.

Table 3 Variables showing a significant association with severity of strokes

Variable, n *(%)*	*TIA, 12 (8.8%)*	*PRIND, 18 (13.1%)*	*CS, 107 (78.1%)*	p *value*[a]
Elective operation	12 (12.8%)	16 (17.0%)	66 (70.2%)	0.003
Urgent operation	0	2 (6.5%)	29 (93.5%)	0.047
Emergent operation	0	0	12 (100%)	0.158
Straight cannula	10 (16.7%)	14 (33.3%)	101 (50%)	0.047

CS: completed stroke; TIA: transient ischaemic attack; PRIND: prolonged reversible ischaemic neurological deficit. [a]Chi-square test.

the brain were performed in 103 patients (75%). After four to six weeks, 24.8% (n=34) of stroke patients had severe residual deficits.

Predictors of stroke

Table 2 displays the univariate relation between stroke versus pre- and perioperative variables ordered by p value. A 95% confidence interval was used to assess univariate predictors of stroke. Known risk factors or symptoms of atherosclerotic disease were age, diabetes, carotid stenosis, aortic calcification, peripheral artery disease, and history of previous stroke. Other variables were related to known risks of cardiac embolism such as pre- and postoperative atrial fibrillation. The use of straight aortic cannulae was also identified as a risk factor for stroke. With the use of bent-tip cannulae, the incidence of strokes decreased to 0.9% versus 1.8% with straight cannulae (χ^2, p=0.026). There was no significant association between the individual surgeon and stroke.

Factors influencing the severity of stroke

The severity of CVAs was classified as TIA (n=12; 8.8%), PRIND (n=18; 13.1%), and CS (n=107; 78.1%). By examining the influence of different pre- and intraoperative variables (Table 3), we found that the use of straight aortic cannulae was associated with more severe CVAs in comparison to bent end-hole cannulae (χ^2, p=0.047). Urgent nature of operation was also associated with more severe CVAs (χ^2, p=0.047), while elective cases were associated with less severe CVAs (χ^2, p=0.003).

Factors influencing the location of strokes

In 132 patients, the location of CVA could be classified as 'right' (39.4%), 'left anterior' (29.5%), 'posterior' (13.6%), or 'bilateral' (17.4%). In five cases, localization could not be established. The occurrence of bilateral or posterior strokes correlated with the use of straight cannulae, but not with the use of bent-tip cannulae (χ^2, p=0.015). Additional factors influencing the location of strokes are listed in Table 4. Bilateral CVAs were frequent after urgent procedures (χ^2, p=0.021), left anterior CVAs were associated with bilateral carotid stenosis (χ^2, p=0.029), right anterior CVAs were correlated positively with aortic valve replacement (χ^2, p=0.026), and hypertension was associated with significantly fewer right anterior CVA strokes (χ^2, p=0.003).

Discussion

The number of studies on the location of CVA after cardiac surgery is limited,[7,11] and they are limited primarily to presence or absence of carotid stenosis.[12–14] Our study, just as that of Ricotta *et al.*, also identified carotid stenosis as a risk factor, but found no correlation between the side of carotid stenosis and ipsilateral stroke.[14] This may implicate other factors such as cardiac or aortic emboli. Our study does not clarify the correlation between bilateral carotid stenosis and left anterior strokes.

The study of Weinstein attributes the higher incidence of left hemispheric territorial CVAs to the use

Table 4 Variables associated with location of stroke

Variable, n *(%)*	*Right, 52 (39.4%)*	*Left 39 (29.5%)*	*Posterior 18 (13.6%)*	*Bilateral 23 (17.4%)*	p *value*
Hypertension	31 (30.7%)	33 (32.7%)	17 (16.8%)	20 (19.8%)	0.003
Urgent operation	6 (19.4%)	11 (35.5%)	4 (12.9%)	10 (32.3%)	0.021
Aortic valve replacement	21 (58.3%)	10 (27.8%)	2 (5.6%)	3 (8.3%)	0.026
Bilateral carotid stenosis	1 (12.5%)	6 (75%)	1 (12.5%)	0	0.029
Cannula type					0.114
Straight cannula	45 (37.5%)	34 (28.3%)	18 (15%)*	23 (19.2)*	
Bent-tip cannula	7 (58.3%)	5 (41.7%)	0	0	

*Bilateral or posterior strokes were significantly more frequent with straight (34.2%) versus bent-tip (0%) cannulae than unilateral right or left hemispheric strokes (66% versus 100%) with $p < 0.015$.

of bent-tip aortic end-hole cannulae, resulting in a jet stream towards the orifice of the left common carotid artery.[7] However, our study could not confirm these findings. The Coanda effect,[15] an application of the Bernoulli principle, which attributes decreased flow in vessels that are not 'jet-streamed', may explain why we have observed a similar number of right anterior strokes. This imbalance of arch vessels perfused with curved end-hole cannulae was shown in an *in vitro* study and related to a suboptimal orientation of the jet stream into the aortic arch.[17] It also has to be considered that in several retrospective studies in which patients with cerebral embolism unrelated to cardiac surgery were analysed, the most frequent site of infarction was also the left anterior circulation, especially the area supplied by the left middle cerebral artery. The asymmetry of branching patterns of the extracranial cerebral arteries was thought to be responsible for this preference.[18]

To our knowledge, there are no studies that compare the incidence of stroke related to the use of the shape of aortic cannulae. Excluding neuropsychological disorders, the overall stroke rate in our study is in the reported range in cardiac surgery.[1] In our study, the use of bent-tip aortic cannulae reduced significantly the incidence of stroke and we did not observe bilateral or posterior infarcts. This difference in location or a reduced embolic load may be the reason for the less severe strokes associated with the use of bent-tip cannulae.

In the study of Benaroia *et al.*, the occurrence of microemboli during CPB, as measured by transcranial Doppler sonography, was not affected by the choice of aortic cannula.[16] In this study, however, the patient population was small and free of peripheral vascular disease, therefore probably with a low risk of atheroembolism from the ascending aorta.

The orientation of the cannula tip in the lumen of the aorta, in relation to the aortic wall, is different for the two cannula types. The jet streams are aimed towards the posterior aortic wall, close to the rise of the innominate artery in the case of straight cannulae, and parallel to the aortic long axis in the case of bent-tip cannulae. The energy dissipation of the flow is greater for bent-tip cannulae due to a parallel orientation of the cannula tip, resulting in a larger distance before the jet stream hits the aortic wall past the supra-aortic vessels. The different orientation of the jet streams may mitigate the even higher peak flow velocities experienced with smaller diameter of bent-tip cannulae in our study (Table 1). This may explain why these cannulae, despite a higher pressure gradient, were associated with a significantly lower incidence of strokes and why no bilateral or posterior strokes were observed in our study.

The study of Barbut *et al.* reported posterior distribution of brain infarcts related to cardiac surgery.[11] This phenomenon was attributed to atherosclerotic plaques in the ascending aorta; only in one patient was the brain infarction attributed to ipsilateral carotid stenosis. The influence as to how different aortic cannulae may cause various intensity and orientation of jet streams was not assessed in this study, but it may be the underlying reason to explain some of the differences observed.

Bilateral transcranial Doppler sonography was used to detect side preferences of cardiac emboli during cardiac surgery. A significantly higher number of high-intensity transient signals were recorded in the right proximal middle cerebral artery.[19] Our correlation between aortic valve replacement and right anterior strokes may be related to preferential embolization of valvular debris into the innominate artery. The association between hypertension and rarity of right anterior strokes remains unclear.

In conclusion, the shape of an end-hole cannula influences the location and severity of strokes. Straight cannulae are associated with significantly more, and more severe, bilateral and posterior strokes than bent-tip cannulae. Therefore, proper use of bent-tip cannulae may be preferential for patients undergoing cardiac surgery.

Limitations of the study

The actual frequency of CVAs may have been underestimated, especially in the cases with subtle neurological deficits when initially emerging from anaesthesia. Aortic calcification was not assessed by ultrasound and received proper documentation only after 1997. The type of aortic cannula was not tested prospectively and was not randomized. However, differences in stroke incidence were evaluated, despite the bent-tip cannulae being of smaller diameter. Our study did not assess the embolic load and distribution of emboli with intraoperative transcranial Doppler sonography, but analysed the clinical neurological outcome of the patients. It is known to be difficult to distinguish between corpusculate and gaseous particles with transcranial Doppler sonography and to derive information from the recorded signals in relation to possible clinical manifestations of a neurological deficit.

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5.3.2. Erhöhte Leukozytenwerte - Ein neuer Risikofaktor für den postoperativen Schlaganfall. (Originalpublikation II)

Albert A, Beller C, Walter J, Arnrich B, Rosendahl U, Priss H, Ennker J (2003). Preoperative high leukocyte count: a novel risk factor for stroke after cardiac surgery. Ann Thorac Surg 75:1550-1557.

Experimentelle Daten lassen vermuten, dass zusätzlich zu den Faktoren Embolie und Hypoperfusion, auch hemorheologische und inflammatorische Faktoren bei der Pathogenese des Schlaganfalles beteiligt sein könnten [siehe Kapital 1.2.]: In der Schlaganfall-Forschung besteht das Problem, dass die Patienten bereits mit dem stattgefundenen Ereignis die Klinik erreichen, und daher hemorheologische und inflammatorische Faktoren erst *nach* Auftreten des Schlaganfalls untersucht werden können. Dann lässt sich nicht mehr differenzieren, ob mögliche Veränderungen Ursache oder Folge des Ereignisses sind. In der Herzchirurgie bietet sich die Gelegenheit solche Laborwerte ein bis zwei Tage vor Auftreten des Schlaganfalls zu untersuchen. Bisher gab es aber noch keine klinischen Untersuchungen, welche Laborwerte kurz vor dem Schlaganfall-Ereignis untersuchten.

Wir führten eine Studie zu den Risikofaktoren eines postoperativen Schlaganfalls durch, es wurden alle von März 1997 bis Dezember 2000 am Herzen operierte Patienten eingeschlossen (n=7483). Neben den Leukozyten (und dem Differenzialblutbild) wurden eine Vielzahl weiterer Patienten-Assoziierter Faktoren, Laborwerte und Operations-Assoziierte Faktoren analysiert, um möglichst viele Störfaktoren (Confounder) im logistischen Model zu kontrollieren. Eine gute Voraussetzung für eine hohe Quantität und Qualität der Daten wurde durch die kurz zuvor fertig gestellte Konstruktion des der DataMart geschaffen [siehe Kapitel 2.1].

Wir fanden in diesem gemischten Kollektiv mit unterschiedlichen Operationsarten eine Schlaganfallrate von 1,7% (RINDs und TIAs eingeschlossen). Erhöhte Leukozytenwerte wurden als ein Risikofaktor für das Auftreten von Schlaganfällen identifiziert. Das Ergebnis bestätigte sich auch für Subgruppen der Patienten, wie der reinen Bypassoperation. Das relative Risiko, einen Schlaganfall zu erleiden, stieg signifikant mit Höhe der Leukozytenwerte: bei Leukozyten-Werten von $\geq$ 8,8 10^9/l betrug die Schlaganfall-Inzidenz 2.1%, bei Leukozyten-Werten $\geq$ 18 10^9/l betrug sie 4.16%. Analysen der Leukozytensubpopulationen zeigten, eine Korrelation der Granulozyten und der Monozyten, aber nicht der Lymphozyten mit dem Schlaganfall. Wir machten weitere erwähnenswerte

Beobachtungen, nämlich 1) dass alle Patienten mit TIAs normale Leukozytenwerte hatten und 2) dass mit ansteigender Leukozytenzahl auch die Schwere eines Schlaganfalles zunimmt; Wir folgerten, dass Leukozyten ein Kofaktor bei der Genese von zerebralen Ischämien sind und bei der Übertretung der Schwelle vom transienten zum manifesten Defizit mitbeteiligt sein könnten.

Unsere Ergebnisse haben dazu beigetragen, die Bedeutung der Leukozyten für die Pathophysiologie der vaskulären Ischämie zu untermauern [Coller 2005], und hatten auch praktische Konsequenzen für den klinischen Alltag: Patienten mit erhöhten Leukozytenwerten sollten, wenn von der kardialen Seite her vertretbar, nicht operiert werden, bevor der zugrundeliegende Infekt behandelt wurde [Selim 2007].

Preoperative High Leukocyte Count: A Novel Risk Factor for Stroke After Cardiac Surgery

Alexander A. Albert, MD, Carsten J. Beller, MD, Jörg A. Walter, PhD, Bert Arnrich, MS, Ulrich P. Rosendahl, MD, Horst Priss, MD, and Jürgen Ennker, MD

Clinic for Cardiothoracic Surgery, Heart Institute Lahr/Baden, Lahr, Germany, Institute of Neuroinformatics, University of Bielefeld, Bielefeld, and Department of Neurology, Regional Hospital Lahr, Lahr, Germany

Background. Stroke after cardiac surgery is a devastating complication. The relationship between white blood cell count (WBC) and perioperative cerebrovascular accident (CVA) has not been investigated. An effort was made to identify how preoperative WBC may relate to CVA development during or after cardiac surgery.

Methods. Prospective data were collected from 7,483 patients who underwent coronary artery bypass grafting or valvular surgery or both. WBC was determined preoperatively and postoperatively. Differentiation of WBC was examined only preoperatively.

Results. There were a total of 125 CVAs (10 transient ischemic attacks [TIAs], 115 strokes). WBC was significantly higher preoperatively and directly postoperatively in patients with stroke. Qualitative changes in preoperative WBC were also found in these patients (χ^2; $p < 0.001$). The predictive power of the stepwise logistic regression model for CVA was greater when preoperative WBC was included. The risk for perioperative CVA increased starting at preoperative WBC of 9×10^9/L ($p = 0.044$) and progressed in higher WBC ranges. WBC had a significant impact on CVA outcome (analysis of variance, $p = 0.001$).

Conclusions. Our studies have established the correlation between high preoperative WBC and stroke during or after cardiac surgery. Furthermore, elevated preoperative WBC was related to the clinical outcome of CVA. Preoperative measures aimed at preventing or treating conditions such as infections that may cause elevated WBC may be beneficial in the prevention of stroke during or after cardiac surgery.

(Ann Thorac Surg 2003;75:1550–7)

Despite different strategies aimed at reducing neurologic injury the incidence of neurologic disorders after cardiac surgery remains high [1]. Several risk factors have been identified [2, 3, 4]. Cerebral hypoperfusion—either global or regional—seems to play a major role in the pathogenesis of perioperative stroke and may be linked to embolism [5]. Hemorheologic and inflammatory changes associated with cardiopulmonary bypass (CPB) may also contribute to the development of stroke after cardiac surgery [5]. There are however no data about the correlation of preoperative quantitative and qualitative changes in the white blood cell count (WBC) with development of stroke during or after cardiac surgery.

Experimental data suggest that leukocytes are involved in the pathogenesis of ischemic brain damage [6, 7]. Numerous studies also demonstrate that recent infection and chronic inflammation are indeed risk factors for cerebrovascular ischemia [8–10]. These studies are based mostly on data obtained from the patient history, antibody titers, and long-term immunologic markers. An epidemiologic study identified a high WBC determined several months to a few years before the onset of stroke as an independent risk factor [11]. No laboratory data are available for the majority of stroke patients before the onset of stroke. Our study examines the possible significance of WBC on the development of stroke during or after cardiac surgery. Also using cardiac surgery as a model, we wanted to contribute to the understanding of stroke in general.

Material and Methods

From March 1997 to December 2000, 8,008 adult patients underwent cardiac surgical procedures at the Heart Institute Lahr/Baden, Germany. Patients who had had thoracic aortic surgery, off-pump coronary artery bypass grafting, and simultaneous carotid endarterectomy were excluded from the study. That left us with 7,483 patients, of whom 5,596 underwent isolated coronary artery bypass grafting (CABG), 567 had CABG with simultaneous valvular procedures, 634 had isolated aortic valve replacements, 190 had isolated mitral valve surgery, 55 had double valve replacements, 75 had redo valve replacements, 252 had redo CABG, and 114 had other major cardiac surgical procedures. Data for quality assessment were collected prospectively on all patients as part of a national quality assessment trial of cardiothoracic surgery ([Quadra] Quality Assurance Data Review Analysis) and cardioanesthesia using standardized protocols of the German Society of Thoracic and Cardiovascular Surgery and Intensive Care Medicine [12, 13]. A technical assis-

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Address reprint requests to Dr Albert, Hohbergweg 2, 77933 Lahr, Germany; e-mail: alexander.albert@heart-lahr.com.

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tant for data collection and medical documentation controlled the data collection and tested the interrater reliability.

Variables such as preoperative medications (class of substances, eg, β-blocker, diuretics), data concerning the operating team (eg, individual surgeon), the degree of carotid stenosis if present (all degrees were recorded but only stenoses with 50% or more were included for the analysis), the degree of aortic arteriosclerosis (graded: none, mild, moderate, severe), and history of neurologic disease (eg, history of CVA or other neurologic diseases) were recorded. WBC was measured preoperatively and directly postoperatively but differential WBC was measured only preoperatively (Automatic Analyzer Sysmex K4500; Sysmex, Hamburg, Germany). Leukocytes were classified as granulocytes, lymphocytes, or as a "mixed group" that included monocytes, basophiles, and eosinophiles. Lower and upper limits of "normal" WBC were 4.3 to 10.8 $\times$ 10^9/L [14]. Yearly controls of blood cell measurements were performed by the Institute for Standardization and Documentation in Medical Laboratories, according to instructions of the German Medical Association. Comprehensive results were obtained the entire time from 1997 to 2001. The data were stored perioperatively in three commercially available electronic databases (Medwork, Datapec, Clinicom, Düsseldorf, Germany), consolidated, and transmitted to a "datamart" system. The laboratory data were implemented automatically in our datamart system. Several plausibility checks during data collection and data consolidation in our datamart system were performed.

For the present study, we analyzed 37 variables from the more than 160 attributes collected for each patient.

Clinical preoperative studies included routine Doppler ultrasonography of the carotid and the vertebral arteries and spirometry. A neurologist examined patients with high-grade carotid stenosis or history of neurologic disorders to assess existing preoperative neurologic deficits and to facilitate a distinction from possible perioperative neurologic events. Assessment of aortic calcification was obtained through intraoperative palpation or direct inspection through the aortotomy or the punch-holes for the proximal anastomoses since 1998. Postoperatively all patients were evaluated for possible neurologic deficits by nurses and doctors. If focal neurologic defects or prolonged decreases of consciousness were detected a neurologic consultation was obtained. Depending on the severity of symptoms, a computed tomography (CT) scan of the brain was performed and interpreted independently by a radiologist and a neurologist. Patients in whom brain damage developed after resuscitation or cardiac arrest were excluded from the study.

Classification of Cerebrovascular Accidents

The clinical characteristics and temporal course of postoperative CVAs were described according to a classification of the National Institute of Neurologic Disorders and Stroke [15]: as transient ischemic attack (TIA) if symptoms lasted less than 24 hours, as reversible ischemic neurologic deficit (RIND) if symptoms lasted longer than 24 hours up to 3 weeks, or as completed stroke if neurologic symptoms persisted beyond 3 weeks. The latter was further classified as minor or major completed stroke to assess the clinical outcome. Major completed strokes were defined as those with subsequent death from stroke or severely affecting ambulation or day-to-day functioning still persisting 4 to 6 weeks after discharge. Minor completed strokes were defined as those with mild residual deficits. RINDs and minor or major completed strokes were summarized in terms of "stroke" in contrast to TIAs in this article. For patients with preexisting neurologic deficits a new CVA was diagnosed if new neurologic symptoms developed or there was obvious prolonged worsening of already existing symptoms. In the course of clinical data analysis, systematic chart review was done for the 125 patients who suffered a CVA.

Perioperative Management

The patients were operated on by 12 different surgeons. The patients received heparin (375 KIE/kg) at the completion of median sternotomy to obtain an activated clotting time in excess of 400 seconds. Cardiopulmonary bypass was established with an ascending aortic cannulation in an area free of atherosclerotic plaque and a single two-stage right atrial cannula (except for mitral valve procedures). Jostra HL 20 heart-lung machines (Jostra, Hirrlingen, Germany) with capillary oxygenators and arterial filters (pore size 40 μm) were used. Roller pumps generated nonpulsatile flow. Target CPB flow was between 90% and 120% of the calculated value (body surface area multiplied by 2.5), the target pressure was 60 mm Hg and higher for patients with known carotid stenoses (60 to 80 mm Hg), maintained with noradrenalin if necessary. Moderate hemodilution (hematocrit 24% to 30%, age dependent) and moderate hypothermia (32°C to 35°C) was used. From 1998 on, patients were kept normothermic (>35°C) during most CABG. Heparin was neutralized by protamine. Aprotinin (2.5 to 5 million KIE) was used in nearly all patients. Patients with low cardiac output or who needed adrenalin more than 0,2 $\mu g \cdot kg^{-1} \cdot min^{-1}$ were placed on intraaortic balloon pump. All patients were treated with a third-generation cephalosporin (cefazolin) before, during, and after surgery.

Statistical Analysis

Univariate comparisons between subjects with and without CVA were performed with χ^2 tests and Fisher's exact test for categorical data and with Spearman's rank order and Kendall's τ test for ordinal data. Continuous variables were evaluated by unpaired Student's t test or analysis of variance (ANOVA). Stepwise forward logistic and linear regression methods were used to determine predictors of CVA. We employed the SPSS v10.0 package (Chicago, IL) for the statistical tests. Model discrimination was evaluated by the area under the receiver operating characteristic (ROC) curve.

Results

Characteristics of Patients With CVA

The prevalence of CVA was 1.7% (n = 125); 65% of these were diagnosed within 72 hours postoperatively. The in-hospital mortality rate was 9% (n = 11) of patients with CVAs versus 2.5% (n = 187) of patients without CVA (n = 7,358). In 50% (n = 62) of the CVA victims a marked alteration of vigilance developed: 41 of those were somnolent, 12 were soporous, and 9 were comatose. Nine patients were reintubated owing to CVA and 35 patients (28%) were maintained on prolonged mechanical ventilation. In 120 patients the CVA was classified as right (40%), left anterior (29.2%), posterior (13.3%), or bilateral (17.5%). In 5 cases localization was not possible. CT scans of the brain were performed in 98 patients (78%). Brain infarction was classified as "borderline" in 6.1% of cases and as lacunar in 9.2%. Twenty percent showed combined territorial and lacunar infarction and 64.7% showed isolated territorial infarction. After 4 to 6 weeks (mean: 35 days) 7.2% of patients with completed strokes had severe residual deficits.

Predictors of CVA

All univariate risk factors (Table 1) were included as dichotomous or ordinal variables in a stepwise logistic regression analysis. There was no association between the individual surgeon and CVA (χ^2, $p = 0.224$).

Preoperative WBC was analyzed in three categories according to the "normal" WBC range: WBC less than 4.3 $\times 10^9$/L, WBC 4.4 $\times 10^9$/L to 10.8 $\times 10^9$/L, and WBC more than 10.8 $\times 10^9$/L. For the first time a high preoperative WBC was identified as one of seven independent predictors of perioperative CVA: use of intraaortic balloon pump, carotid stenosis, history of stroke, preoperative atrial fibrillation, preoperative WBC, postoperative atrial fibrillation, and age (Table 2). The area under the ROC curve was calculated as 0.741 (95% confidence interval [CI]: 0.696 to 0.786). Excluding the preoperative WBC reduced the area under the ROC curve to 0.737 (95% CI: 0.691 to 0.783). To validate the clinical importance of the WBC effect an additional stepwise logistic regression analysis was carried out only for patients with isolated CABG (n = 5,498; 84 CVAs; CVA rate, 1.5%) in our study population (Table 3). This CVA score identified except for postoperative atrial fibrillation the same independent risk factors: the influence of preoperative WBC on the discriminative ability of the model was even higher in this subgroup (area under the ROC curve: 0.771 [95% CI: 0.716 to 0.826] with preoperative WBC versus 0.761 [95% CI: 0.706 to 0.815] without preoperative WBC). Additionally a stepwise logistic regression analysis was carried out only for patients with stroke (TIA excluded, see Appendix Table 1). This CVA score identified eight independent risk factors including again preoperative WBC: the discriminative ability of this model was good (area under the ROC curve 0.748; 95% CI 0.69 to 0.79).

Relative Risk for CVA Depending on Different Preoperative WBC Ranges

Figure 1 shows the WBC histograms for the two groups with and without CVA. For the WBC groups up to 6 $\times$ 10^9/L there was a lower frequency for CVA; for WBC more than 9 $\times 10^9$/L the CVA frequency was progressively growing. The relative CVA risk for several top percentile ranges of WBC were computed (Table 4). We found a significantly lower relative CVA risk for low preoperative WBC levels (WBC $< 6.2 \times 10^9$/L), Patients with a preoperative WBC more than 9 $\times 10^9$/L had a significantly elevated relative risk for perioperative CVA. To capture the clinical relevance we conducted the following "gedankenexperiment." We assumed the underlying causes for elevated preoperative WBC could be treated and WBC could be reduced to an average level (the average level to be reached is the mean of the group without CVA approximately 7 $\times 10^9$/L (6.7 $\times 10^9$/L to 7.7 $\times 10^9$/L)): the number of potentially preventable CVA would be as high as 10%.

Analysis of WBC Differentiation Count

Preoperative differentiation of WBC of patients with CVAs showed significantly higher preoperative granulocyte and "mixed" cell counts. There was a nonsignificant drop in the lymphocyte count. Results are displayed in Table 5.

Clinical Manifestation of CVA

CVA was classified as TIA in 10 patients, as RIND in 16 patients, as minor completed stroke in 78 patients, and as major completed stroke in 21 patients. Clinical manifestation of CVA varied significantly with preoperative WBC ($p < 0.001$ ANOVA; Fig 2). The severity of CVA outcome correlated the level of preoperative WBC. Compared with patients suffering RIND (mean WBC 8.5 $\pm$ 2.2 $\times 10^9$/L SD) or completed strokes (mean WBC for minor completed strokes: 8.7 $\pm$ 3.7 $\times 10^9$/L SD; mean WBC for major completed strokes: 9.3 $\pm$ 4.5 $\times 10^9$/L SD) lower values were measured for patients suffering a TIA (mean WBC: 6.9 $\pm$ 0.8 $\times 10^9$/L SD; $p < 0.001$; *t* test). Patients with RIND or TIA had lower values than patients with minor or major strokes ($p = 0.012$; *t* test). In patients with TIA, WBC was even lower than in patients without CVA (mean WBC: 7.8 $\pm$ 2.7 $\times 10^9$/L SD; $p = 0.005$, *t* test). Mean WBC differences between major versus minor completed strokes were of marginal significance ($p = 0.078$; *t* test).

Characteristics of Patients According to WBC

A stepwise forward linear regression model showed a very poor impact of evaluated preoperative variables on preoperative WBC ($R = 0.176$, see Appendix Table 2). There was a low inverse correlation for age, mitral stenosis, and aortic insufficiency. There was a low direct correlation between higher WBC and diabetes, peripheral artery disease, the emergent nature of the operation, postinfarction ventricular septal defect, pulmonary hypertension, and chronic obstructive pulmonary disease (COPD).

Table 1. Preoperative, Intraoperative, and Postoperative Univariate Predictors of Cerebrovascular Accident (CVA) Ordered by CVA Rate

		Stroke Rate			
Variable	Percent/Total	Present	Absent	*p*-Value	OR
Postinfarction ventricular septal defect	0.1%	10%	1.7%	0.04	2.1
Severe aortic calcification	3.8%	7.2%	1.6%	<0.001	4.8
Intraaortic balloon pump	1.1%	6.2%	1.6%	0.001	3.9
History of stroke	8.5%	4.7%	1.4%	<0.001	3.5
Asymptomatic carotid stenosis (≥50%)	10.5%	4.6%	1.3%	<0.001	3.5
Preoperative atrial fibrillation	6.8%	4.5%	1.5%	<0.001	3.0
Aortic cross-clamp time (min)				0.245	
<60	58.3%	1.5%	—		—
60–120	40.7%	1.8%	—		—
>120	1%	4.2%	—		—
Mitral stenosis	1.5%	3.6%	1.6%	0.109	2.3
WBC preoperatively ($\times 10^9$/L)				0.018	
<4.3	2.2%	1.2%	—		—
4.3–10.8	89.7%	1.5%	—		—
>10.8	8.2%	3.3%	—		—
Peripheral artery disease	10.2%	3.1%	1.5%	0.001	2.1
Pneumonia	0.4%	3.1%	1.7%	0.417	2.0
NYHA class				0.062	
I	18.2%	1.8%	—		—
II	32.1%	1.0%	—		—
III	43.2%	1.9%	—		—
IV	6.5%	2.9%	—		—
Ejection fraction (%)				0.01	
<30	6.3%	2.8%	—		—
30–55	31.1%	2.1%	—		—
>55	62.6%	1.4%	—		—
Previous cardiac surgery	4.9%	2.7%	1.6%	0.108	1.7
Active endocarditis	0.5%	2.7%	1.7%	0.455	1.6
Age (years)				<0.001	
<60	24.5%	0.5%	—		—
60–70	38.6%	1.5%	—		—
>70	37.0%	2.6%	—		—
Mitral valve surgery	12.8%	2.6%	1.5%	0.015	1.7
Pulmonary hypertension	4.6%	2.6%	1.6%	0.167	1.5
COPD	19.4%	2.5%	1.5%	0.004	1.7
WBC postoperatively (30 min) ($\times 10^9$/L)				0.042	
<4.3	2.6%	2.5%	—		—
4.3–10.8	57.7%	1.3%	—		—
>10.8	39.7%	2.1%	—		—
History of myocardial infarction				0.584	
>6 months	22.0%	1.8%	—		—
>3 months	11.3%	1.7%	—		—
<3 months	7.1%	1.7%	—		—
<24 hours	1.7%	2.4%	—		—
Postoperative atrial fibrillation	47.3%	2.3	1.1	<0.001	2.1
Diabetes mellitus	26.8%	2.3%	1.4%	0.006	1.6
Operation				0.051	
Elective	76.4%	1.5%	—		—
Urgent	17.2%	2.3%	—		—
Emergent	6.4%	2.1%	—		—
Operating time (min)				0.039	
<180	28.1%	1.3%	—		—
180–240	49.3%	1.6%	—		—
>240	22.6%	2.2%	—		—

Table 1. (Continued)

		Stroke Rate			
Variable	Percent/Total	Present	Absent	*p*-Value	OR
Aortic valve replacement	20.7%	2.2%	1.5%	0.07	1.5
Body mass index (kg/m^2)				0.137	
<20	1.8%	2.2%	—		—
20–25	27.1%	2.0%	—		—
>25	71.1%	1.5%	—		—
Total CPB time (min)				0.026	
<90	50%	1.3%	—		—
90–120	31.3%	1.9%	—		—
>120	18.8%	2.1%	—		—
Female sex	29.4%	2.1%	1.5%	0.041	1.4
Aortic stenosis	13.9%	2.1%	1.6%	0.224	1.1
Hypertension	68%	1.9%	1.3%	0.054	1.5
Intraoperative ultrafiltration	1.5%	1.8%	1.7%	0.893	1.1
LV aneurysmectomy	1.6%	1.6%	1.7%	0.969	0.9

COPD = chronic obstructive pulmonary disease; CPB = cardiopulmonary bypass; LV = left ventricle; NYHA = New York Heart Association; OR = odds ratio; WBC = white blood cell count.

Comment

Our study confirmed the well-known risk factors for perioperative CVA such as age, history of stroke, preoperative and postoperative atrial fibrillation, carotid stenosis, diabetes, and intraaortic balloon pump [2–4]. In this context, embolism and hypoperfusion as interrelating factors seemed to play a major role [5]. Although hemorheologic factors have also been suspected to play a role in the development of stroke after cardiac surgery the main focus remained the well-known inflammatory response after CPB and its impact on endothelial function [5].

We now have identified a new predictor of stroke occurring during or after cardiac surgery: preoperative WBC. Preoperative WBC remained an independent risk factor also in cases with isolated CABG. The risk for perioperative CVA increased starting at preoperative WBC of 9×10^9/L and progressed in higher WBC ranges. In addition we demonstrated that the level of preoperative WBC strongly correlated with the severity of the stroke outcome.

So far studies of patients with stroke unrelated to cardiac surgery could only demonstrate a correlation between leukocyte count after stroke onset and infarct size or initial stroke severity [16, 17]. Patients with completed stroke showed a significantly higher aggregation of leukocytes than patients with TIA, suggesting that changes in aggregability of leukocytes may play a role in the evolution of the disease [18]. Our finding that the preoperative leukocyte level had an impact on CVA outcome is concordant with animal experiments in rats in which decreased WBC (induced by the antineoplastic agent vinblastine before cerebral ischemia) reduced infarct size and enhanced evoked potentials [6]. Interestingly patients with a TIA had lower preoperative WBC than patients without completed strokes.

In an attempt to establish the possible causes of elevated preoperative WBC we performed a stepwise for-

Table 2. Multivariate Logistic Regression Analysis for Cerebrovascular Accident[a]

Variable	*p* Value	OR = exp(β),	95% CI
Intraaortic balloon pump	0.008	3.621	1.398–9.376
Carotid stenosis	0.000	2.655	1.753–4.022
History of stroke	0.000	2.582	1.662–4.010
Preoperative atrial fibrillation	0.000	2.376	1.465–3.852
WBC preoperatively	0.004	1.981	1.236–3.176
Age	0.000	1.718	1.305–2.262
Postoperative atrial fibrillation	0.038	1.515	1.023–2.243

[a] All cases (n = 7,483, intercept $\alpha = -7.40$).

CI = confidence interval; OR = odds ratio; WBC = white blood cell count.

Table 3. Multivariate Logistic Regression for Cerebrovascular Accident[a]

Variable	*p* Value	OR = exp(β)	95% CI
Preoperative atrial fibrillation	0.000	4.116	2.190–7.737
Intraaortic balloon pump	0.038	3.736	1.072–13.019
Carotid stenosis	0.000	3.043	1.867–4.961
History of stroke	0.000	2.747	1.618–4.663
WBC preoperatively	0.001	2.615	1.500–4.558
Age	0.000	1.822	1.307–2.540

[a] Only isolated CABG (n = 5,498, intercept $\alpha = -8.10$).

CI = confidence interval; OR = odds ratio; WBC = white blood cell count.

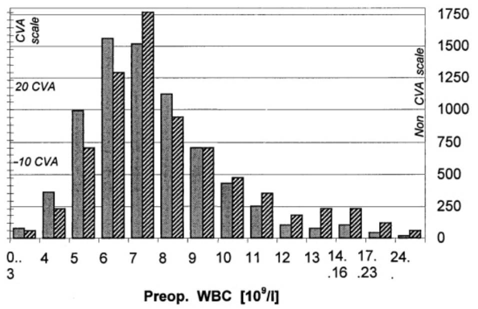

Fig 1. White blood cell count (WBC) histograms with and without cerebrovascular accident (CVA), scaled to equal size. The WBC values were truncated (eg, "5" bin indicates the interval [5, 6]) and some bins were aggregated to remain visible. The CVA columns are magnified relative to patients without CVA by the factor 58.86 (equals ratio no-CVA/CVA cases) such that the area sums were equal (the null hypothesis of equal stroke risk would approximately yield columns of pair-wise same size). Gray bars = *no CVA;* hatched bars = *CVA. (Preop. = preoperative.)*

Table 5. Preoperative Granulocyte, Lymphocyte, and Mixed Cell Count in Patients With and Without Cerebrovascular Accident (CVA) (× 10^9/L)

	No CVA (Mean ± SD)	CVA (Mean ± SD)	*p* Value
Granulocytes	5.25 ± 2.22	6.18 ± 3.55	<0.001
Lymphocytes	1.94 ± 1.23	1.81 ± 0.76	0.253
Mixed cells[a]	0.58 ± 0.3	0.67 ± 0.34	0.002

[a] Monocytes, eosinophils, basophils.

ward linear regression analysis. The correlation found was too low to exclusively explain the reason for the elevation of WBC. In other studies some of these factors were associated with leukocytosis. Higher WBC in patients with peripheral artery disease possibly reflects the immunoinflammatory nature of arteriosclerosis [19]. A low-grade inflammation with relatively elevated leukocytes, C-reactive protein, and fibrinogen levels was also shown to be associated with both peripheral artery disease and ischemic vascular events [8]. Elevated WBC in diabetic patients is well described and postulated to be caused by microvascular inflammation [20]. In our study, age was inversely correlated with WBC. That is probably an indication of declining immune response with age [21]. Preoperative high WBC may also be caused by myocardial infarction (acute ventricular septal defects) or by emergent operations leading to a stress response [22].

The differentiation of WBC in our patients with stroke showed a significant elevation of neutrophils and probably monocytes. That could be a marker for severe arteriosclerosis [19]. Infections may also cause this elevation of neutrophils and monocytes, an event that could predispose these patients to CVA. Severe preceding infection, either pneumonia or endocarditis, could only be found in 43 patients (0.5%), two of whom suffered a stroke postoperatively. Mild or subclinical infections were not assessed in this study. That may explain why patients with stroke showed an elevated WBC. Both viral and bacterial infections of the respiratory and urinary tract especially have been identified as predisposing risk factors for brain infarction [8–11]. The average time interval between infection and stroke onset was 1 week [10]. Even low-grade inflammation was associated with vascular risk factors and may contribute to the risk of end-organ ischemia [8].

The link between infection and stroke is still not fully understood. The underlying mechanism may be an altered leukocyte rheology causing aggregation that leads to obstruction of small vessels [18]. The release of vasoreactive or cytotoxic mediators could cause injury to endothelial cells further potentiating the ischemic damage [7]. Infections also seem to affect the protein-C pathway and endogenous fibrinolysis leading to a proco-

Table 4. Relative Risk for Cerebrovascular Accident (CVA) Depending on Different Preoperative White Blood Cell Count (WBC) Ranges

Group by WBC Quantile	WBC Range (10^9/L)	CVA/All Cases in Group	Percent CVA	Relative Risk[a]	*p* Value	Preventable CVA Number	Preventable CVA Percent Total[b]
Lower 25%	<6.2	20/1746	1.1	0.62	0.029		
25%–50%	(6.2, 7.4)	34/1938	1.8	1.07	0.402		
50%–75%	(7.4, 8.8)	29/1822	1.6	0.93	0.429		
Upper 25%	≥8.8	42/1977	2.1	1.41	0.044	12.3	10
Upper 10%	≥10.4	23/834	2.7	1.78	0.012	10.4	8
Upper 5%	≥11.9	14/378	3.7	2.37	0.004	8.0	6
Upper 2.2%	≥14	7/167	4.2	2.60	0.022	4.3	3
Upper 1.1%	≥16	5/85	5.9	3.63	0.014	3.6	3
Upper 0.5%	≥18	3/44	6.8	4.16	0.037	2.3	2

[a] Relative risk = (percentage CVA in group)/(percentage CVA not in group); here approximate odds ratio. [b] Potentially preventable CVAs in group under the assumption that the preoperative WBC could be reduced to an average level: (1-1/relative risk) × number of CVA in group.

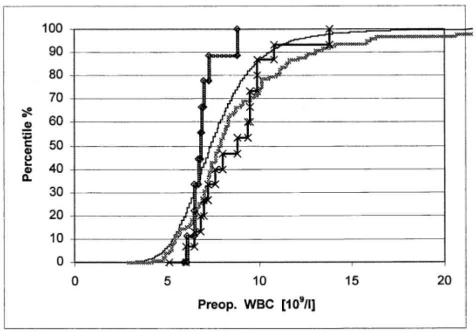

Fig 2. Accumulated frequency diagram for different severity stages of cerebrovascular accident (CVA) *(patients without CVA as reference) in relation to preoperative white blood cell count* (WBC) 10^9/L. Solid line = *no stroke;* fuzzy line = *completed stroke;* X line = *RIND;* diamond line = *TIA.* (Preop. = *preoperative; RIND = reversible ischemic neurologic deficit; TIA = transient ischemic attack.)*

agulant state [9]. Elevated systemic C-reactive protein levels associated with chronic periodontal infections could also contribute to the higher risk for stroke in these patients [23]. Furthermore a persistent inflammatory response was found with higher leukocyte and neutrophil levels in stroke survivors. In these cases fibrinogen also remained significantly elevated and was associated with increased risk for recurrent vascular events [24]. That may explain why a previous stroke is one of the major risk factors for stroke after cardiac surgery [2–4].

In several studies COPD, a univariate predictor in our study, was found to be an independent risk factor for stroke after cardiac surgery [2–4]. It was postulated that retained carbon dioxide alters the cerebral vasoregulation and compromises the ability to compensate for embolic events [2, 3]. Prolonged mechanical ventilation in these patients was suspected to cause a decreased cerebral perfusion and hypoxia [3]. Elevated hemoglobin could not be proved to be a possible risk factor for stroke in these patients [4]. In the context of our findings it is also possible that acute exacerbation of chronic obstructive pulmonary disease with elevated WBC may contribute to the development of stroke. In this process elevation of plasma fibrinogen and increased serum interleukin-6 levels have been suspected to be responsible for the increased cardiovascular morbidity and mortality [25].

Additional studies assessing the role of mild or subclinical infections (eg, periodontal, urinary tract, and pulmonary infections) may help to determine whether elevated WBC per se is a risk factor or is but a marker for an underlying condition that causes both elevated WBC and stroke during or after cardiac surgery.

In conclusion we found that a high preoperative WBC was an independent risk factor for CVA during or after cardiac surgery. Additionally, the preoperative WBC was related to CVA outcome. This phenomenon should be further investigated. Patients with a high leukocyte count before cardiac surgery may benefit from treating the underlying cause of the leukocytosis.

Limitations of the Study

The actual frequency of CVA may have been underestimated in patients with subtle neurologic deficits. Although we did not assess severity of stroke by using a standardized published stroke scale, our classification was simple and clinically oriented. The role of postoperative leukocytosis was not investigated further because it would have been difficult to interpret. We did not study other variables of infection such as C-reactive protein or fibrinogen levels. Aortic calcification was not assessed by ultrasonography and received proper attention only after 1997. While our study established a correlation between WBC and stroke occurring during or after cardiac surgery, it did not define WBC as being a risk factor per se or as a marker for underlying causes.

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Appendix

Table 1. Multivariate Regression Analysis, All Cases (n = 7,483, intercept $\alpha = -7.67$), Only for Strokes Excluding Transient Ischemic Attacks

Variable	Significance	OR = exp(β)	95% CIC
Intraaortic balloon pump	0.009	3.572	1.366–9.345
Carotid stenosis	0.000	2.530	1.631–3.926
History of stroke	0.002	2.155	1.340–3.466
Preoperative atrial fibrillation	0.004	2.135	1.278–3.567
Preoperative WBC	0.003	2.079	1.284–3.366
Age	0.000	1.692	1.272–2.251
Peripheral artery disease	0.032	1.685	1.046–2.713
Postoperative atrial fibrillation	0.019	1.634	1.082–2.467

CIC = confidence interval; OR = odds ratio; WBC = white blood cell count.

Table 2. Factors Correlating Preoperative White Blood Cell Count, Stepwise Linear Regression Analysis (R = 0.176)

Variables	B	95% CIC
Postinfarction ventricular septal defect	2.002	0.36–3.64
Mitral stenosis	−0.853	(−1.4)–(−0.31)
Mitral insufficiency	0.831	0.53–1.13
Emergent operation	0.543	0.44–0.65
Pulmonary hypertension	0.441	0.14–0.74
Peripheral artery disease	0.42	0.22–0.62
Aortic insufficiency	−0.371	(−0.58)–(−0.16)
COPD	0.287	0.13–0.44
Diabetes	0.277	0.14–0.41
Congestive heart failure	0.145	0.004–0.29
Age	−0.018	(−0.024)–(−0.011)

CIC = confidence interval; COPD = chronic obstructive pulmonary disease.

5.3.3. Online-Überwachung der operativen Sterblichkeit durch „Variable Life Adjusted Displays”. Eine wertvolle Methode für das Benchmarking und frühzeitiges Erkennen negativer Entwicklungen in der Herzchirurgie (Originalpublikation III)

Albert A, Walter J, Arnrich B, Hassanein W, Rosendahl U, Bauer S, Ennker J (2004a). On-line variable live-adjusted displays with internal and external risk-adjusted mortalities. A valuable method for benchmarking and early detection of unfavourable trends in cardiac surgery. Eur J Cardiothorac Surg 25:312-319.

Eine Möglichkeit, Manipulationen an der Aorta und damit iatrogen verursachte Hirn-Embolien bei der Bypassoperation zu minimieren, ergibt sich dann, wenn die Operation ohne Herz-Lungen-Maschine durchgeführt wird. Diese Operation ist allerdings ein technisch anspruchsvolles Operationsverfahren, das unter bestimmten Bedingungen auch mit einem erhöhten Risiko für den Patienten einhergehen kann und einer speziellen Qualitätskontrolle bedarf. Hier ist es wichtig, ein Überwachungsverfahren zu haben, welches noch in der Implementierungs-Phase ungünstige Verläufe so rechtzeitig anzeigt, dass Zeit zum Reagieren bleibt und Komplikationen für weitere Patienten vermieden werden. Wir haben dazu ein System der Überwachung herzchirurgischer Ergebnisse entwickelt, welches auf der Methode der Variable Life Adjusted Displays (VLADs) beruht. Mit diesem, von einem Londoner Pionier der Kinderherzchirurgie (M. de Leval) aus der industriellen Prozesskontrolle in die Herzchirurgie übertragenen Verfahren, werden herzchirurgische Leistungen über die Zeit kumulativ aufgetragen und bewertet. Im Falle, dass der Patient überlebt, steigt die Kurve, im Falle des Versterbens fällt sie. Das Ausmaß des Anstiegs oder Abfalls hängt von dem vorhergesagten Operationsrisiko des Patienten ab: Je höher dieses ist, desto stärker steigt die Kurve an, und je niedriger es ist, desto stärker fällt die Kurve im Falle des Versterbens des Patienten ab.

Wir haben die VLAD-System in unseren klinischen Alltag integriert und bezüglich folgender Funktionen weiterentwickelt:

Als Referenz wird erstmals der EuroSCORE verwendet; weil aber durch den EuroSCORE das Letalitätsrisiko häufig überschätzt wird, haben wir als zusätzliche Referenz eine Kalibrierung des EuroSCORE auf die Klinik-spezifischen Letalitäten durchgeführt. Dadurch können die Ergebnisse der jeweiligen Analysen mit den internen wie externen (Benchmarking)

Ergebnissen verglichen werden. Zusätzlich können jeweils die 30-Tage- und die Krankenhaus-Letalität gesondert gewählt werden.
Die VLADs basieren auf dem DataMart und werden entsprechend tagesaktuell automatisch aktualisiert. Ein gestern verstorbener Patient führt heute bereits zu einem Abfall der Kurve.
Der VLAD Kalkulator ist multimodal, es können je nach Auswahl des Anwenders VLAD Kurven für bestimmte Operateure, Operationsarten und für bestimme Zeitintervalle gewählt werden.
VLAD-Kurven sind Teil eines Online-Berichtswesens. Sie sind, wie die anderen Komponenten des Online-Berichtswesens im Intranet von allen Ärzten abrufbar; so kann jeder Arzt seine eigenen Performanz-Charts ansehen (bei Bedarf für bestimmte Operationsarten und/oder Zeitintervall), der Chefarzt und Administrator (Autor) dagegen können die Ergebnisse aller Chirurgen einsehen.
Mit Hilfe der VLAD-Kurven waren wir in der Lage, typische Probleme bei der chirurgischen Ausbildung, in der Leistungsentwicklung einzelner Chirurgen oder temporäre Leistungsknicks der gesamten Abteilung, z.B. nach einem Wechsel des Teams oder des Managements zu erkennen.
Nach Einführung der OPCAB-Methode ließ sich mit Hilfe der VLADs eine Lernkurve darstellen. Aber auch im weiteren Verlauf zeigten die Performanzkurven keinen positiven Trend (gegenüber der internen Referenz). Dies führte neben anderen Problemen, welche durch Fallkonferenzen (Bypassverschlüsse), Analysen der Lebensqualität oder weiterführende Studien (niedrigere Flüsse im CX-Gebiet [Hassanein 2005]) identifiziert wurden, sowie einer schlechtere Bezahlung im DRG-System, zu einem weitgehenden Verlassen des OPCAB-Verfahrens.

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On-line variable live-adjusted displays with internal and external risk-adjusted mortalities. A valuable method for benchmarking and early detection of unfavourable trends in cardiac surgery☆

A.A. Albert[a,*], J.A. Walter[b], B. Arnrich[b], W. Hassanein[a], U.P. Rosendahl[a], S. Bauer[a], J. Ennker[a]

[a]*Clinic for Cardiothoracic Surgery, Heart Institute Lahr/Baden, Lahr 77933, Germany*
[b]*Institute of Neuroinformatics, University of Bielefeld, Bielefeld, Germany*

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Abstract

Objective: Benchmarking and early detection of unfavourable trends. **Methods**: We implemented a dedicated project-orientated data warehouse, which continuously supplies data for on-line computing of the variable live-adjusted displays (VLADs). To calculate the expected cumulative mortality, we used the multi-variate logistic regression model of the EuroSCORE model. In addition to the external EuroSCORE standard, we calculated a centre-specific risk score for internal standards by analysing the data of 9135 patients, which enables both internal and external comparisons. The VLADs are embedded into the multi-purpose web-based information portal, so that the physicians can investigate several types of VLADs interactively: performance of different types of surgery and individual surgeons for different time intervals. We investigated clinically important events such as modification of operative techniques and personnel changes of the team by the VLADs. **Results**: We found transient declines in the performance curves during major changes in patient management, indicating that systemic—rather than accidental or patient related factors—were involved in the mortality risk. The internal standard line represents these clusters more clearly than the external line. We evaluated examples of how periods of increased risk could be monitored by the VLAD curves: (1) the introduction of OPCAB surgery; (2) training of surgeons; (3) staff changes and staff-related management. **Conclusions**: On-line VLADs based on a day-to-day updated database, displaying both internal and external standards, are a helpful visualisation tool for earlier detection of unfavourable trends. They enable the surgeon teams and clinical management to take countermeasures at an early stage.

Keywords: Variable live-adjusted displays; Risk adjustment; EuroSCORE; Cumulative sum method; Data warehouse

1. Introduction

Clinicians are encouraged to improve their methods of investigation and analysis of outcomes, which still tend to be underdeveloped in comparison to methods available in industry [1]. In cardiac surgery, outcome data are usually presented as 30 day or in-patient mortality. Nowadays, it is generally accepted procedure to adjust mortality rates for the estimated perioperative risk [2,3]. The ability of the risk adjustment models on an individual basis is limited. Predictive models cannot consider all patient characteristics that may have an influence on surgical mortality. Generally, they do not consider non-patient-related factors which are known to influence clinical practice and contribute to the outcome such as knowledge and experience of individual staff members, work environment, organisation and management factors [1]. In order to identify these contributory factors, it appears very helpful to consider the temporal occurrence of clinical incidents. A promising method of continuous monitoring of surgical results was introduced to cardiac surgeons in 1994 [4]. It was previously developed in industry for monitoring quality on a production line. For this

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* Corresponding author. Tel.: +49-7821-925-367; fax: +49-7821-925-253.
E-mail address: alexander.albert@heart-lahr.com (A.A. Albert).

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cumulative sum method (CUSUM) cases were plotted sequentially on the horizontal axis and the plot moves up one unit for each death to represent the cumulative sum of deaths. A series of surgical failures related to neonatal arterial switch operations was detected by characteristic movements of the resulting curve. The method was refined by incorporating success and failure as well as previously estimated risk using the Parsonnet Score for each case [5,6] and further by adding prediction intervals to indicate increasing departures from expected mortalities [7]. There is one observational study that used variable live-adjusted display (VLAD) successfully to compare the performance of two individual hospitals in treating patients with myocardial infarction [8]. Beyond this pioneering work, there is only little experience with VLADs in medicine.

2. Method

Building a web-based information portal required several steps: first, we implemented a dedicated project orientated data warehouse (data mart), followed by the calculation of VLAD charts according to published techniques [5,6] and subsequently developed a technique to provide multi-purpose VLAD charts on-line.

2.1. Data warehouse/data mart

All heart operations performed at the Heart Institute Lahr/Baden from January 1996 on were analysed continuously. Data for quality assessment were collected prospectively on all patients as part of a national quality assessment trial of cardiothoracic surgery (Quality Assurance Data Review Analysis, Quadra) and cardio-anaesthesia using standardised protocols of the German Society of Thoracic and Cardiovascular Surgery and Intensive Care Medicine [9,10]. A technical assistant for data collection and medical documentation controlled the data collection and tested the inter-rater reliability. Preoperatively, the data is fed into three independently operating commercial hospital information systems (Medwork, Datapec, Clinicom). From there, our data warehouse extracts, transforms, and consolidates the data in order to build up a large, comprehensive database, which appears to the investigator as a single data source. Mortality within 30 days was meticulously recorded with a completeness of more than 99% using a specific procedure based on questionnaires and phone calls to the patients after discharge.

2.2. Calculation of VLADs

The 18 EuroSCORE risk variables could be continuously determined from our data warehouse. In order to determine the estimated percentage of death, the items and additive weights were derived from the simple additive EuroSCORE model, which uses only dichotomous or ordinal data [11]. The second, centre-specific risk score was calibrated to the locally observed mortality by rescaling the data of 9135 patients from 1st January 1996 to 1st April 2002, such that the sum of the expected mortality (EM) of all individuals equals the total number of observed mortalities (OM). For all patients the EM was in the range of 0.002–0.1 [12]. VLADs were created by continuous display of operative results. In the case of a successful operation, the curve goes up by the value of EM for this patient; if the patient dies, the curve decreases by the value of $1 - \text{EM}$. If the patient was at a high risk of perioperative death, the surgeon's mortality figures are not unduly penalised but mortality figures are penalised when a low-risk patient dies. The results for every single patient are cumulated and altogether display the performance. The expected cumulative mortality minus the actual cumulative mortality is called 'net live saved'.

2.3. Web-based information portal

In our institution, VLADs are part of a multi-purpose intranet information portal, made available to all physicians via intranet. It provides various statistics on operative results and allows the export of various anonymous patient data for all authorised physicians. VLADs can be selected for several operating types, time intervals and/or individual surgeons. The access to VLADs displaying individual surgeon's performance is limited to the surgeon himself and specially authorised persons. Our VLAD plot simultaneously displays curves, which are based on predictive mortalities derived from the EuroSCORE publications and curves after recalibration. VLADs as well as all statistics presented at the web-based information portal are derived directly from the data warehouse and are updated automatically.

We established weekly meetings of our physicians for a joint analysis of adverse outcomes. VLADs were correlated to clinical events and factors possibly influencing clinical practice and contributing to adverse events. They are interpreted regularly by the staff. From this study, we present examples that should be of general interest.

3. Results

Overall, 30-day mortality for 14 487 cases was 2.2%. The area under the receiver-operating characteristic (ROC) curve before and after recalibration was 0.75 and 0.78, respectively. In nearly all VLADs, the external standard line elevated continuously, since OM were lower than the EM of EuroSCORE and, on average, the internal curve moves along the zero line. A transient decline in a curve, with an accumulation of adverse events, is called a cluster. These clusters were easier to detect in the internal line because, in cases of transient declines, the external line shows only a small directional change in the ascending slope. We found clusters during major changes in patient management.

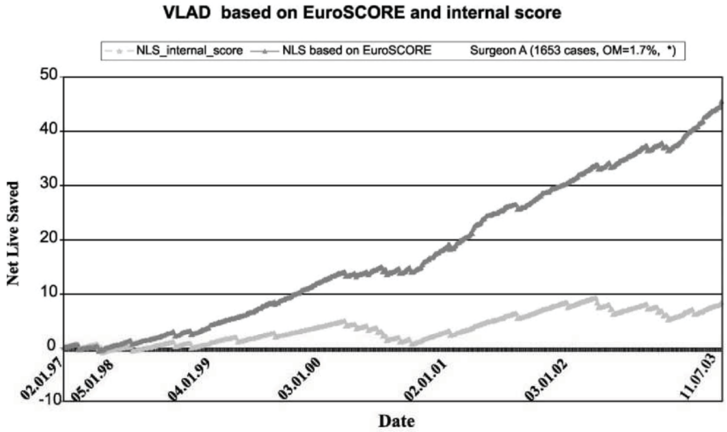

Fig. 1. During the training of a Surgeon A, two periods with an accumulation of adverse events occurred: the first after starting with training, the second cluster 4 years later (about 600 cases). Additionally, two clusters were observed during the year 2002. See also Figs. 4–7.

During the training period of the surgeons, clusters occurred at the onset of training and after an uneventful period of 300–600 operations a second cluster surprisingly occurs (Figs. 1 and 2). The learning curve cluster after starting with cardiac surgery revealed OM between 2.9 and 2.2% (Surgeon A, 5/170 operations; Surgeon B, 5/224). The second learning curve cluster shows mortalities between 4.7 and 3.3% (Surgeon A, 8/170; Surgeon B, 4/120) and a decrease in net lives saved (internal score) by 4.1 (Surgeon A) and 1.1 (Surgeon B). The learning curve after introduction of OPCAB surgery is characterised by a cluster with an observed mortality of 3.9% (5/129) and a decrease in net lives saved of 2.86 (Fig. 3). The overall performance of the cardiosurgical clinic showed the most impressive clusters during the year 2002 (Fig. 4), independent of the performance of individual surgeons (Figs. 1, 5 and 6). During 1416 operations, 54 mortalities occurred (3.8%) and net lives saved (internal score) decreased by 24.2. Net lives saved of the two surgeons A and B decreased from 1.2 to − 8.2 and 3.4 to − 3.2, OM was 6.7% (21/315, Surgeon C) and 4.6% (13/285, Surgeon D) during this time period. Also surgeon A showed a marked decrease of the performance during the year 2002. Net lives saved decreased from 9.2 to 5.3 and OM was 4.2% (8/190). Fig. 7

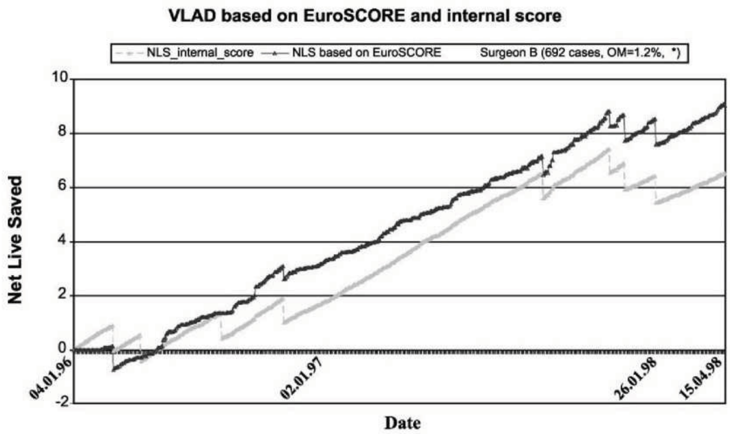

Fig. 2. During the training of a Surgeon B, two periods with an accumulation of adverse events occurred: one during the first year and a second cluster after 4 years (about 600 cases).

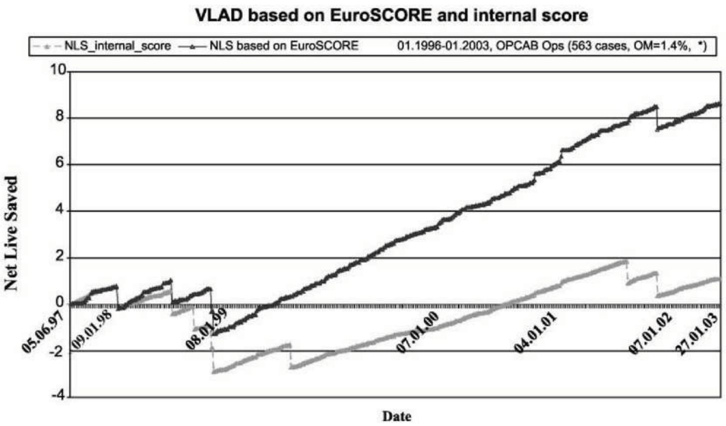

Fig. 3. A learning curve in OPCAB is displayed: there is an accumulation of adverse events during the first 150 OPCAB operations.

shows how the performance increased from January 2001, beginning with the decrease in risk-adjusted in-hospital mortality (increase of the VLAD curve). In-hospital mortality was zero and net lives saved increased by 6.3.

4. Discussion

These VLAD charts revealed increased frequencies of fatalities, which correlate with specific circumstances and alterations in patient care: onset of surgeons' training, delegation of more responsibilities to trainees, learning of new surgical techniques and changes in staff and general and clinical management. These performance patterns are invisible when analysed by simple grouping in specific time periods.

For example, the annually performed risk-adjusted statistics could not demonstrate any difference in 30-day mortality between OPCAB versus on-pump. However, motivated by the results of the VLAD curves, we performed retrospective studies of the individual patients, which revealed an increased rate of perioperative myocardial infarction due to bypass graft thrombosis and incomplete revascularisation. This finding supports the impression given by the VLADs, which attributes the cluster of adverse events after starting with OPCAB not to the risk

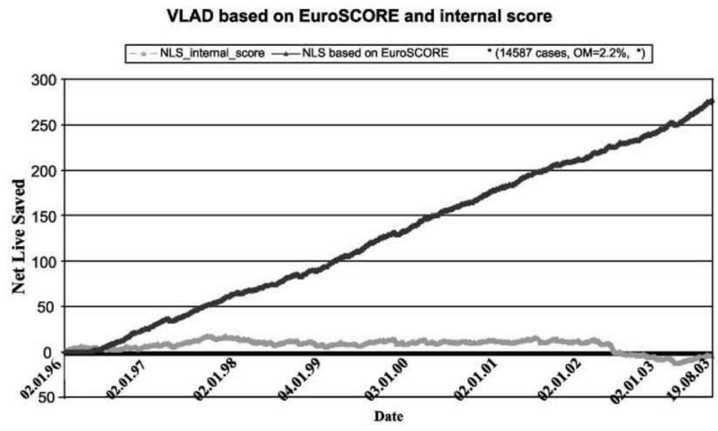

Fig. 4. The overall performance of the cardiosurgical clinic is displayed. Clusters were found in the year 2002. Improvement concerning the staff on the ICU, and adaptation to the changes in organisation and management resulted in an increase in performance.

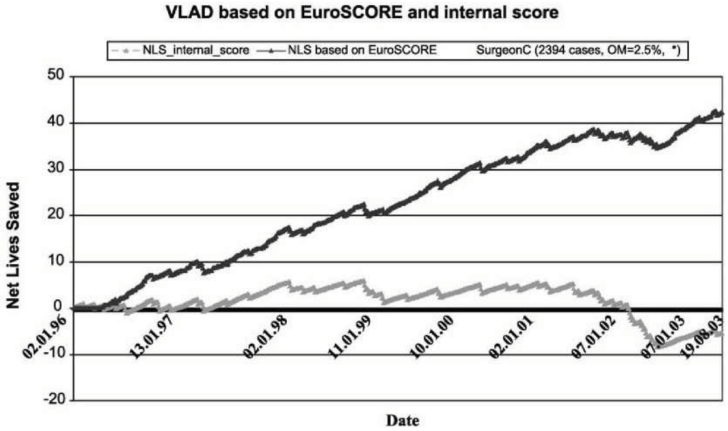

Fig. 5. Experienced Surgeon C showed a marked decrease in performance during the year 2002, which is accompanied by the decline in the overall performance of the cardiosurgical clinic. See Figs. 1, 4, 6 and 7.

of the patients but to the learning ability of the surgeons. At that time, various surgeons performed OPCAB surgery primarily in high-risk patients (>80 years, severely decreased pulmonary function, preoperative stroke, etc.), so that complications were interpreted individually rather than systemically as an effect of a learning curve in OPCAB surgery. Later, when OPCAB surgery was limited to three surgeons who specialised in this, performance increased. Probably a continuous monitoring of performance by VLADs at that time would have detected the learning curve earlier. Another observation concerning a learning curve in OPCAB was made using non-risk-adjusted CUSUM analysis [13].

The training of cardiac surgeons showed similar patterns of performance. When considering annual statistics we could not identify any difference in outcome between trainees, registrars, and consultants. This is in line with studies analysing the effect of surgical training on outcome in cardiac surgery [14–16], which could not prove any detrimental effect on patient outcome in operations performed by trainees. However, the observed clusters of fatalities at the beginning of the training and later after 200–600 operations were identified in several surgeons. This corresponds with the original report studying VLADs in individual surgeons, which found clusters at the beginning of training in two surgeons, and a later cluster

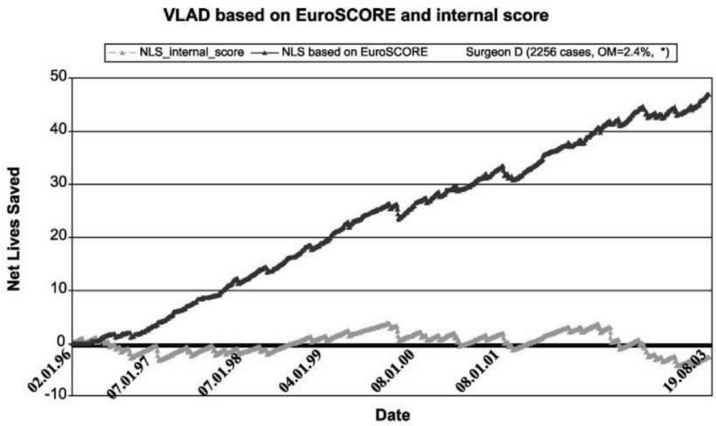

Fig. 6. Experienced Surgeon D showed a similar curve to that of Surgeon C (Fig. 5) with a marked decrease in performance during the year 2002, which is accompanied by the decline in the overall performance of the cardiosurgical clinic. See also Figs. 1, 4 and 7.

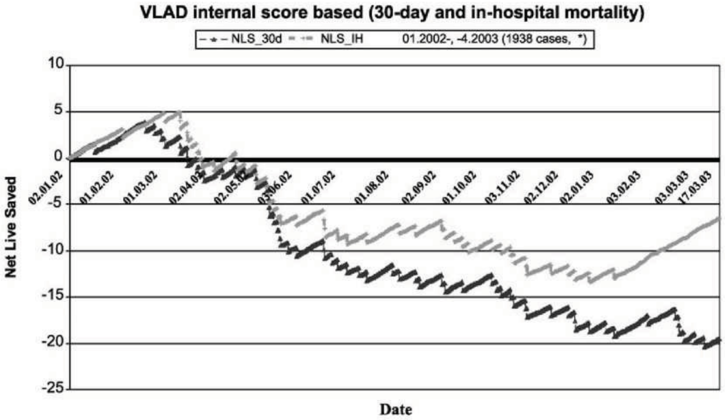

Fig. 7. Regaining of overall performance started in January 2003 with the decrease of in-hospital mortality (increase in net lives saved based on internal score and in-hospital mortality).

after 250–350 cases in one surgeon [5]. One report applying CUSUM retrospectively to display the 10-year performance of one surgeon also identified a cluster during the first year of training [17]. Technical error, inexperience and poor judgement are readily reflected in operative mortality in cardiac surgery, conditions which are probably involved in the emergence of these first clusters.

The decline in performance after 300–600 operations we observed in our trainees most likely reflects a drop in supervision, greater optimism and overestimation of the trainee's abilities as far as difficult cases were concerned. Our observation led to an increased supervision of trainees as well as of apparently more experienced colleagues.

The third example reveals a decrease in overall performance of the cardiosurgical department in the year 2002. VLADs suggest that the increase in mortality is not only a consequence of the higher risk of the patients but of other contributory factors. In the year 2002, our facility, especially the ICU-team, experienced significant and relevant changes in staff and staff-related management. Measures were taken to restructure the ICU staff, and to improve organisational and management changes, which resulted immediately in regaining good overall performance.

What is strongly recommended for all situations when information is drawn from clinical databases [18] is the participation of the physicians in the process of data acquisition and analysis. This applies in particular to the VLADs. In order to avoid a misuse of incomplete or inaccurate data we built a data warehouse, which allows the inspection and verification of the whole data integration process. Additionally, case-based verification tools were developed and plausibility checks are performed automatically. The power of the VLADs depends on the model of EM and therefore, on the choice of the underlying risk score. In the first instance, this concerns the type of risk model. Studies applying external risk scores to centre-specific populations reported a wide range of areas under the ROC curve (0.67 [19] and 0.831 [20]).

Secondly, this concerns the local adaptation or recalibration of risk scores. The human visual system can detect subtle absolute slope trends around the horizontal line much better than higher slope trends, e.g. $-1°/+1°$ versus $20°/22°$ elevation angle. Therefore, we recalibrated the EuroSCORE expected mortalities to fit the observed centre-specific mortalities. This allows for easier visual recognition of the periods of performance changes.

Despite these refinements, we still observe inaccuracies of some VLADs, such as an overall decline in performance in valve operations in comparison to bypass operations. Thus, for an additional improvement in VLADs it would appear advantageous to fit the individual weightings of the EuroSCORE to the population specific for our facility or to alter the EuroSCORE parameter mix. For example, we could recently show how renal function can be better assessed by replacing the variable creatinine by the creatinine clearance, which significantly increased the area under the ROC curve [12].

Optimal adjustment for the clinic specific population requires the development of a risk model beyond the EuroSCORE and another time window of the risk score outcome than 30-day mortality. It was demonstrated that the hazard of dying after CABG induced by the preprocedural condition and the procedure itself continues to exist for 2 months beyond the date of the procedure [21]. It was confirmed that the risk incurred by the highest risk patients is likely to be underestimated by 30-day mortality [22]. The suggestion was made to postpone the endpoint of 30-day mortality to 1 year post-operative for a case mix [23]. In this context, it must be pointed out that precise comparisons between therapies and appropriate medical decision making requires follow-up intervals as long as possible as well as more sophisticated data exploration and analysis [24]. The more uniform the patient population is, the more feasible is the application of more complex, time-related analysis for continuous monitoring of surgical results. Furthermore, it has to be considered that higher the costs and the more special parameters included in the scoring model the less suitable it is for interclinic benchmarking [23]. VLADs regain the biggest benefit in a large case mix. The generation of VLADs with both external and internal standards enables us to apply the more complex techniques of risk adjustment to the internal standard and to maintain a simple score like the EuroSCORE as a 'common language'.

In order to specify how much variation in the plot is expected under good surgical performance, and hence a deviation from the expected, should be a cause for concern, prediction intervals were incorporated into the VLADs [7,25]. The normal distribution of mortality rates within a sizeable sequence of operations was used to construct nested prediction intervals [7]. The prediction intervals were colour coded and superimposed onto the VLAD chart to indicate increasing departures from EM. Ref. [25] designed CUSUM graphs which 'signals' if sufficient evidence has accumulated to indicate that the surgical failure rate has substantially changed. The run length until the CUSUM signifies the deterioration in performance and the discriminative ability of the test depends on the choice of the control limits, which can be varied according to the medical context and the heterogeneity of the case mix. Other investigators do without prediction intervals [6,8]. They stress that the interpretation of VLADs requires the consideration of other qualitative trends and obvious changes in patient management is more important. Furthermore, a failure to act on the qualitative trend observed until a significant P value has been achieved could result in the avoidable loss of lives.

5. Summary

VLADs enable us to monitor different aspects of surgical performance and to discover non-patient-related factors contributing to surgical risk. In order to monitor different aspects of patient management, VLADs should be accessible for all team members and provide the selection based on several aspects, e.g. operating procedures, individual surgeons, or time periods. To solve the choice problem of generalised score for interclinic benchmarking versus a specialised intraclinic score, we recommend supporting multiple VLAD chart types in a readily accessible intranet information system.

On-line VLADs based on a day-to-day updated database are a helpful visualisation tool for earlier detection of unfavourable trends, enabling the surgeon teams and clinical management to take countermeasures at an early stage.

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Appendix A. Conference discussion

Dr G. Laufer (*Innsbruck, Austria*): What was the mean EuroSCORE in your institution, because it is well known that if the EuroSCORE is rather low that the risk of the patient is overestimated with a classic EuroSCORE, which you could avoid using the logistic EuroSCORE?

Dr Albert: We used the simple additive EuroSCORE without continuous data, which we considered sufficient as external standard. But we performed recalibration of the EuroSCORE for a more accurate internal standard by fitting the expected mortalities of the EuroSCORE to our observed mortalities. Therefore the internal standard demonstrates better our results. So I suggest to go even further steps beyond the EuroSCORE to develop a clinical score.

Dr Laufer: But what was your mean EuroSCORE, for example, for the year 2002?

Dr Albert: I don't have the data now.

Dr Laufer: Because that reflects a little bit the risk profile of your patients.

Dr Albert: Yes, but it is calculated together with all VLADs and included automatically within them. We did not present these numbers, from which expected mortalities of VLADs are calculated, because we preferred here to show graphics rather than tables.

Dr B. Buxton (*Heidelberg, Vic., Australia*): We also use the VLAD system for monitoring early changes. I wonder whether you have looked at adapting this to other outcome measures such as wound infection or stroke, these creep up on you sometimes more subtly than you think, and I wonder whether that would also be a good outcome to measure using this technique?

Dr Albert: Excuse me?

Dr Buxton: Have you adapted this system to the assessment of stroke or perhaps, more importantly, wound infections?

Dr Albert: Yes, we looked for some complications, trying to find a correlation with the rise of mortality. The results are not yet clear so I didn't like to present them here. Often they go parallel to the mortality data sometimes they arise earlier. We used as evidence of complications the length of stay in an intensive care unit more than 7 days, we looked for the stroke rate, bleeding and for postoperative CK-MB greater than 50.

Dr G. Rizzoli (*Padova, Italy*): To me this is just another quality control chart.

Dr Albert: Yes, it is.

Dr Rizzoli: I really don't understand how you can attribute to a single surgeon results that depend from the entire process of patient's care. We know that patients die not only because of the surgeon's performance in the operative room, but also because of the standard of care of the environment. So, did you do a multivariate analysis to isolate if the single surgeon was an incremental risk factor or not?

Dr Albert: As you know, the surgeon has a great impact on the outcome of the patients, and his responsibility goes further beyond the operating room. I showed in the last example that it is not always the surgeon but there were a lot of contributory factors, it is the team and the staff on the ICU which contributes to the outcome, and this becomes clear in our last examples presented here.

Dr T. Carrel (*Berne, Switzerland*): Can you tell us a little bit what kind of consequences you draw from your examination and how fast are you able to react when you see a cluster coming in, if you have an on-line analysis?

Dr Albert: It is not a method for reglementation or punishment. As I told you every surgeon can view his own VLADs, the overall performance of the clinic and the performance concerning different types of surgery. Mostly the interpretation of the VLADs is really easy and it is easy to get a consensus because they correlate with known changes in patient care. Every surgeon or member of the team has to think about what he can change. I showed you in the last example, we employed more qualified staff on the ICU and we discussed other problems.

Dr Laufer: Do you know if you are allowed or the chief of the institution in Germany is allowed to analyse the data for an individual surgeon in this manner or does he need the permission from the individual surgeon? It is the case in Austria according to the data safety law or 'daten schutzgesetz' as we call it in Austria.

Dr Albert: Yes, from the beginning we discussed this issue and all surgeons agreed that they could view their own VLADs, not the VLADs of other colleagues, but the chief can view all. But I told you, it is not a system for punishment.

5.3.4. Analyse der Effektivität eines interaktiven multimodalen CME Fortbildungskurses auf die Einstellung zu und Anwendung von OPCAB (Originalpublikation IV)

Albert A, Peck EA, Wouters P, Van Hemelrijck J, Bert C, Sergeant P (2006). Performance analysis of interactive multimodal CME retraining on attitude toward and application of OPCAB. J Thorac Cardiovasc Surg. 131:154-62.

Unsere bisherigen Erfahrungen mit der OPCAB-Operation ließen vermuten, dass die von uns angewendeten Techniken unzureichend waren und die Chancen des Verfahrens möglicherweise nicht richtig genutzt wurden. Aus der internationalen Literatur war aber bekannt, dass dieses Verfahren die Chance bietet, bei Hochrisikopatienten die Inzidenz von Schlaganfällen zu senken, bei gleichbleibender Qualität der koronaren Bypässe [Sergeant 2004, Pushkas 2004]. Als sich die ökonomischen Rahmenbedingungen des DRG-Systems im Jahr 2004 änderten, wurde in unserer Klinik beschlossen, dieses Verfahren wiedereinzuführen. Zuvor sollte aber eine bessere OPCAB-Technik trainiert werden. Voraussetzungen für eine Wiedereinführung waren, dass das neue Verfahren: 1) anwendbar auf ein breites Spektrum der Bypasspatienten, einschließlich der Hochrisikopatienten, sein sollte, 2) eine durchgehend stabile Hämodynamik unter Vermeidung von Hypotonien und Zuständen mit Low Cardiac Output Syndrom garantiert werden sollte, 3) es keine oder nur eine geringe Anzahl von Konversionen zur HLM-OP gibt, 3) Anzahl und Qualität der Anastomosen dem konventionellen Verfahren in nichts nachstehen und, 4) die Operation reproduzierbar und erlernbar ist.

Das OPCAP-Verfahren, so wie es in Leuven/Belgien angewendet und gelehrt wird, weist offensichtlich diese Kriterien auf. Es werden dort verschiedene Arten von Trainings-Programmen angeboten, angefangen bei Zwei-Tageskursen über einmonatige Praktika bis zu einem vollen Weiterbildungsjahr. Insgesamt hatten bis dahin mehr als 400 Chirurgen aus aller Welt diesen Kurs besucht. Es hatten sich jedoch Zweifel gebildet, inwieweit die trainierten Chirurgen in der Lage waren, das Gelernte in die Praxis umzusetzen und dauerhaft als neue Methode in ihren Kliniken zu etablieren. Zu diesem Zweck studierten wir 50 Teams die zum 2-tägigen OPCAB Training nach Leuven kamen. Wir erfassten vor Beginn des Trainings mittels Fragebögen Charakteristika des jeweiligen Teams wie etwa dessen Zusammensetzung (Chirurg, Anästhesist, OP-Schwester), Ausbildungsstand und Erfahrung mit OPCAB, Spezialisierungen, Einstellung zu OPCAB, vermutete (Kontra-)Indikation zu OPCAB, Charakteristika der Herkunftsklinik, etc). Wir verglichen die Angaben mit den Antworten unmittelbar nach dem Training und 6 Monate später.

Es zeigte sich, dass nach dem Training die OPCAB-Anwendungs-Raten durchschnittlich um 25% zunahmen (von 49% ± 32% auf 23% ± 28% (P <0.0001)), eine Konversion zur HLM seltener vorkam (von 3.5% ± 5% auf 1.3% ± 3% (P=0.006) und die Einstellung zu OPCAB signifikant positiver wurde (mehr Vorteile für Patienten, weniger Kontraindikationen). Das Training führte auch zu einer größeren Korrelation zwischen positiver Überzeugung und der OPCAB-Anwendungs-Raten.

Allerdings waren die Unterschiede zwischen den Teams so eklatant, sodass wir uns fragten, welche Faktoren für eine erfolgreiche Umsetzung innovativer Technik (oder das Scheitern) verantwortlich sind und welche Einflüsse auf die Entscheidungsprozesse des Chirurgen eine Rolle spielen könnten.

Zuerst analysierten wir die Bedeutung verschiedener Trainingsmodalitäten anhand bekannter Lerntheorien und unserer Daten: kognitives Training (Diskussion von OPCAB-Ergebnissen und der vermeintlichen Kontraindikationen) war beispielsweise wichtig, um die Einstellungen gegenüber OPCAB zu ändern; so glaubten nach dem Training mehr Chirurgen mittels OPCAB einen Vorteil für die Patienten erreichen zu können. Zu den Methoden des kognitiven Trainings gehört auch eine Systematisierung und Standardisierung der Methode sowie die Definition von Lerninhalten; die Bedeutung manuellen Trainings sollte durch intensive praktische Übungen außerhalb des Operationssaals verstärkt werden.

Ergebnisse von Studien über die Ausbreitung minimal-invasiver chirurgischer Techniken und Innovationen im Industriebereich zeigten, dass neben den Trainingsmodalitäten die Umsetzungsprozesse einer Reihe von weiteren Einflussfaktoren unterliegen. So identifizierten wir diverse, die OPCAB-Ausbreitung stimulierende Faktoren (wie die. Beteiligung eines Anästhesisten am Training) und hemmende Einflüsse (wie die fehlende Unterstützung des Klinikleiters, Spezialisierung auf andere Bereiche der Herzchirurgie) und neutrale Variablen (wie das Alter des Chirurgen).

Das Erlernens einer sicheren und reproduzierbaren OPCAB-Technik, das Studium der OPCAB-Trainingsmodalitäten und der möglichen Implementierungsstrategien zeigten sich alles zusammen als wichtige Voraussetzungen für die dauerhafte Etablierung des OPCAB-Verfahrens in der klinischen Routine.

Performance analysis of interactive multimodal CME retraining on attitude toward and application of OPCAB

Alexander Albert, MD,[a] Eric A. Peck, MD,[b] Patrick Wouters, MD, PhD,[c] Jan Van Hemelrijck, MD, PhD,[c] Christophe Bert, MD, PhD,[c] and Paul Sergeant, MD, PhD[a]

See related editorial on page 14.

Objective: The transfer of tacit and codified knowledge on a surgical technique is studied in a consecutive cohort of teams participating in interactive multimodal continuing medical education (CME) retraining in off-pump coronary artery bypass (OPCAB).

Methods: Fifty teams of 1.3 ± 0.5 surgeons and 1.1 ± 1.9 anesthetists visited 2.2 ± 0.7 days. Variables describe the pre-visit cardiac activity and OPCAB attitude, complexity score (10 frequently cited complexity criteria), application, and conversion rate. The multimodal approach to knowledge transfer included interactive discussions (commitment; resistances; levers and process of change; methods; outcome; resource optimization), active participation in 3.8 ± 1.3 unselected cases (anchor-stitch, enucleation techniques), low-fidelity bench model (shunt placement, anastomotic technique), and CD-ROM. Exit end points included OPCAB attitude and complexity score. Late end points (3 months) included OPCAB attitude, complexity score, and application rate.

Results: OPCAB was considered, upon exit, beneficial for all patients by 90% of the teams (versus 29 % pre-visit), but by only 62 % of the teams at 3 months. The complexity score downgraded at exit from 3.6 ± 2 (pre-visit) to 1.2 ± 1 ($P < .001$) but increased again at 3 months to 1.6 ± 1 ($P = .001$ versus pre-visit and $P = .001$ versus exit). The 3-month OPCAB rate of the surgeons was 49% ± 32% versus 23% ± 28% pre-visit ($P < .0001$). This was influenced by the pre-visit OPCAB rate and education, as well as by the post-visit changes in complexity scores and attitude. The conversion rate toward cardiopulmonary bypass improved from 3.5% ± 5% (pre-visit) to 1.3% ± 3% (3 months, $P = .006$).

Conclusions: The multimodal OPCAB re-training resulted in a substantial increase of the application, concomitant with a decrease in conversion. The positive impact on attitude and complexity score, at exit, was somewhat reduced in the following clinical confrontation.

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From the Department of Cardiac Surgery, University Hospital Gasthuisberg, Leuven, Belgium,[a] the Division of Cardiac Surgery, The Johns Hopkins Hospital, Baltimore, Md,[b] and the Department of Anesthesia, University Hospital Gasthuisberg, Leuven, Belgium.[c]

The Katholieke Universiteit of Leuven, Belgium, had an educational agreement with Medtronic and Guidant, covering the studied CME activity and for most of the visiting teams. Both industrial partners had no interaction with study design, data collection, data analysis, or manuscript

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Address for reprints: Prof Dr Paul Sergeant, Cardiac Surgery Department, Gasthuisberg University Hospital, Herestreet, B 3000, Leuven, Belgium (E-mail: paul.sergeant@uz.kuleuven.ac.be).

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The first coronary bypass operation (CABG) was performed without the assistance of extracorporeal circulation[1] (ECC). The technique was exceedingly challenging with an unstable surgical field and the constant threat of ischemic complications and the risk of a technically inferior anastomosis. With the advent of the cardiopulmonary bypass circuit, CABG procedures were safer, repeatable, and teachable. In recent years, industry has developed devices allowing a safe, high-quality CABG procedure to be performed without the assistance of ECC. Many surgeons have adopted this technique of off-pump coronary bypass (OPCAB) as part of their surgical armamentarium or as a new concept applicable to all CABG patients. Some units[2] have taken a years-long and gradual approach to implementing this new technology by gradually expanding the patient-spectrum and surgeons; other teams have used retraining and guidance by expert centers to accelerate this

Abbreviations and Acronyms

CABG = coronary artery bypass grafting
CME = continuing medical education
CMEST = Continuing Medical Education of Surgical Technologies
ECC = extracorporeal circulation
OPCAB = off-pump coronary artery bypass
SWOT = strengths, weaknesses, opportunities, threats

process. Very few cardiac surgeons have been trained in these techniques during their residency program.[3] The unique technical challenges of OPCAB grafting have raised concern that adoption of OPCAB may lead to poorer outcomes during each surgeon's learning curve.[4,5] As yet, studies have focused on training residents[6-8] in the OPCAB procedure whereas limited study has aimed on how to most effectively retrain experienced cardiac surgeons.

The Katholieke Universiteit of Leuven reengineered toward OPCAB in all patients and for all surgeons in October 1999.[9,10] Since that date, it provided OPCAB training and retraining, as well, for residents as for experienced surgeons in different formats, based on well-studied and defined educational backgrounds. Between January 2000 and January 2004, 294 multimodal individualized trainings, given to 379 different surgeons and anesthetists, preceded this study. It is the intention of this study to investigate the performance of this format and provide a model and guidance for similar educational venues on the application of this or other new technologies.

Materials and Methods

Study Design

Fifty consecutive visiting teams were enrolled in the study from February through November 2004. Informed consent was obtained from the contact individual for each group. Data were collected by means of three questionnaires.

The initial data form (Appendix 1) was completed on the team's arrival at the hospital, prior to any interaction. This included their OPCAB benefit attitude and their OPCAB complexity score. The OPCAB benefit attitude identified the spectrum of patients (low-risk, high-risk, all patients) they believed receive the most benefit from OPCAB. The OPCAB complexity score identifies 10 anatomic and physiologic conditions commonly considered complexity variables for OPCAB. These included redo operation, the presence of left main disease, severe left ventricular hypertrophy, low ejection fraction, intramural or intraseptal coronary vessels, posterolateral wall coronary vessels, sequential arterial grafts, recent infarct (within 7 days), and an unstable ST segment. The total number of positive responses was calculated as "complexity score." After the visit, the Exit Questionnaire (see Appendix 2) was completed. The 3-Month Follow-Up Questionnaire (Appendix 3) gave insight into the late performance after the training.

Educational Basis

The Leuven CMEST (Continuing Medical Education of Surgical Technologies) has been based, over the years preceding the current analytic project, on the science of knowledge management and technology implementation. Three core elements formed its basis: the taxonomy of learning objectives, the theory of adult learning, and the dynamic theory of organizational knowledge creation.

The *taxonomy of learning objectives*[11] identifies knowledge, skills, and attitude. Knowledge is gained by the digestion of information and its transformation through the process of learning. Skills require the development of psychomotor competencies, a process based on regular practice, expertise motivation, and ongoing training. Attitude refers to how knowledge and skills are combined in the care of patients, including clinical judgment, decision making, and the values of professional behavior.

The *theory of adult learning*[12] integrates cognitive and individualized elements. Cognitive elements[13] focus on internal mental processes, solving real problems. Therefore, perception, reasoning, and understanding are valued more than memory. CMEST was individualized[14] because of the different stages of experience preceding the training, the different expectations, and the individual learning styles.

The *dynamic theory of organizational knowledge*[15] explains the process from knowledge creation by the individual to its integration within the organization. Codified knowledge[16] refers to knowledge that is transmittable in formal, symbolic language, whereas tacit knowledge is hard to articulate, acquired through experience or participation, often context specific. The interaction between surgery and anesthesia is a typical example of tacit knowledge. Tacit and codified knowledge exist along a spectrum and are not mutually exclusive. The transfer of these different natures of knowledge can be through socialization (tacit-tacit), through combination (codified-codified), through externalization using metaphors and analogies (tacit-codified), or through traditional learning methods (codified-tacit).

Knowledge Transfer Process

The knowledge transfer process, consistent over the study interval, was structured in a mind map. The faculty consisted of one surgeon and, alternating, one of three senior anesthetists. After completion of the entry form, well-defined learning objectives were discussed in the first hours of the first day and before surgery. The learning objectives started with a SWOT analysis (strengths, weaknesses, opportunities, threats) of CABG, the need for, the process, and the management of change. This was followed by a discussion of the reengineering: multidisciplinary interaction, monitoring, anesthetic management and conditioning, surgical technique subdivided in teachable components, and finally the actual implementation for all patients and all surgeons. This discussion was guided by slide presentations, animations, and video sequences. Subsequently, the first day, the surgeons scrubbed in and the anesthetists participated in two unselected OPCAB cases, performing well-defined teaching objectives: multidisciplinary interaction, anesthetic management, deep stitch placement, cardiac enucleation, and manipulation. The sequential approach of the retraining is best demonstrated by the enucleation technique. It is first described verbally, then in animation, followed by video, by expert cognitive modeling on the human in the operating theater,

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TABLE 1. Team and retraining variability

Number of teams (N)	50
Visiting team structure	
Surgeons	1.3 ± 0.5
Anesthetists	1.1 ± 1.9
Nurses	0.1 ± 0.2
Originating unit	
CABG annual N cases (% of total cardiac activity)	647 cases (62% of cardiac activity)
	19% (range 0-100; median 14%)
OPCAB activity (% of CABG)	3.4% ± 5% (range 0-20)
OPCAB conversion rate toward CPB (% of OPCAB)	
Visiting surgeon	
CABG annual N cases	180 ± 38 cases
OPCAB activity (% of CABG)	23% (mean 44 ± 18 cases; median 5 cases)
At entry	
OPCAB attitude	29% beneficial for all 4% beneficial for low risk 67% beneficial for high risk
OPCAB complexity score	3.6 ± 2
Retraining activity	
Number of days	2.2 ± 0.7
Number of OPCAB cases	3.8 ± 1.3
Number of conversions seen	0 ± 0

and finally repeated (over the different patients) nonexpert modeling by the visiting surgeon corrected by the expert. The different OPCAB procedures were linked by interactive discussions between expert and scholars about procedural variability and organizational aspects of perfusion and nursing. Virtual training was simultaneously addressed by having team members practice shunt insertion and anastomotic techniques in low-fidelity training models.

Day 2 starts again with expert-scholar interaction about the cognitive and motor skills issues of day 1, as well as economic aspects, real-time quality control monitoring systems, outcome analysis, and finally early and late outcome data of our own population. The acquired OPCAB knowledge was reinforced with two additional unselected cases. The CME ended with a wrap-up discussing the organizational and psychologic issues the team would encounter at return in their units. The exit report was completed and a CD-ROM with the complete slide presentation and OPCAB bibliography provided to assist in institutional education.

Team Variability

Fifty teams of surgeons, anesthetists, and nurses from 16 countries were retrained during 2 days (Table 1). The teams came at their own initiative through word of mouth. The originating institutions were mostly academic (68%). The originating units had an average cardiac surgery practice of 1000 cases (range: 175-3375), with 7.0 ± 4.6 staff surgeons and 1.9 ± 2.6 licensed surgeons without staff position. Information about their early post-CABG morbidity and mortality (Appendix 1) seemed unavailable or incomplete in 76% of the teams, even after repeated requests post hoc. The visiting teams worked together several days a week and some had participated in different formats of OPCAB retraining, preceding the current one. Complex enucleation methods, using sling techniques in combination with apical suction and anastomotic area stabilization, were less commonly used (34%); routine shunting was more commonly used (60%). The average OPCAB application rate of the staff surgeons not participating in the training was only 8% before training, whereas it was 23% for the visiting surgeons. The most frequently cited teaching expectation was multivessel arterial OPCAB revascularization (90%).

Most teams were uncertain about the beneficial effect of OPCAB, as well, on target population as on specific outcome improvement. There was no correlation between pre-CMEST OPCAB attitude and OPCAB application.

The OPCAB complexity score (Table1 and Figure 1) cited most frequently intraseptal and intramural vessels, and unstable ST segment as OPCAB complexity variables.

The team variability influenced the Complexity Score at entrance (R^2 =.37; P <.001): Surgeons not using a sling support combined with an apical suction device had more contraindications for OPCAB, as well as those working in smaller units (less than 1000 cases/year). In contrast, surgeons with a higher annual rate of CABG and surgeons with a history of OPCAB education (interactive discussion, live demonstration) had fewer contraindications.

The decision about retraining was taken by the individual in 64%, by the team in 22%, and by the departmental director in 14% of the teams. Only 4% of the teams funded the retraining expenses (travel and lodging) from personal or institutional resources; the other teams were supported by the industry. The industry signed an educational agreement with the K. U. Leuven.

Follow-up and Statistical Analysis

Late follow-up was complete for all teams, but labor-intensive (average > 5 contacts). Additional variability was calculated indirectly from available variability (eg, the average OPCAB application rate in a unit of the nonparticipating staff surgeons). The OPCAB attitude analysis used matched-pair analysis, after ordinal transformation. The analysis applied univariate and multivariate non–time-related methods (linear and logistic regression) and variable transformations (eg, nominal into ordinal, continuous into nominal, and continuous into mathematical transformations) to obtain optimal relations between studied outcomes and variability.

Results

At Exit

The OPCAB *attitude* at exit was (P <.001) influenced by the training; OPCAB was considered beneficial for all patients by 90%, for the low-risk patients only by 2%, and for the high-risk patients only by 6% of the teams, and 2% were uncertain. No teams reduced (pretraining versus at exit) the beneficial group level from all to a smaller subset. The OPCAB complexity score at exit was 1.24 ± 1, strongly reduced (P <.001, mean difference –2.4) versus at entry.

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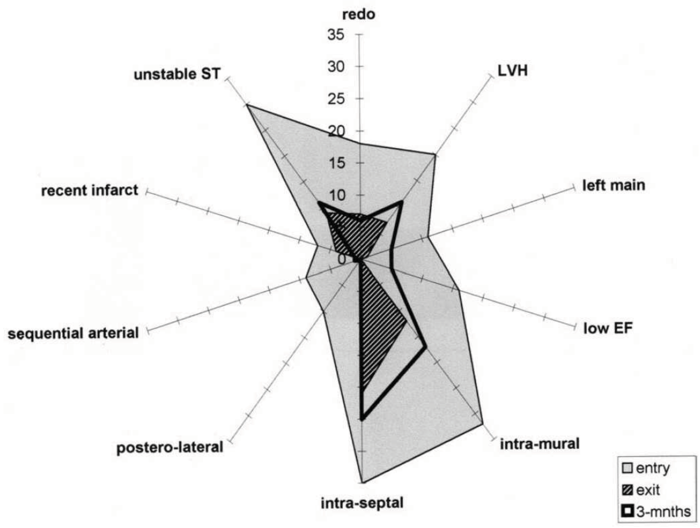

Figure 1. The 10 most frequently cited complexity criteria, by their frequency, cited at entry, at exit. and at 3 months. *LVH,* Left ventricular hypertrophy; *EF,* ejection fraction.

The OPCAB complexity variables most frequently cited at exit were intraseptal vessels and intramural vessels. Figure 1 depicts these 10 most frequently cited complexity criteria versus their prevalence before the retraining. The inferolateral and posterolateral location of coronary anastomoses (10 teams at entry), as well as the sequential arterial grafting (9 teams at entry) and low ejection fraction (16 teams at entry), disappeared from the list at exit.

At 3 Months

The OPCAB *attitude* at 3 months remained strongly influenced by the training ($P <.001$, versus at entry). OPCAB was considered beneficial for "all patients" by 64%, for the low-risk patients by 10%, and for the high-risk patients by 26% of the teams. Fifteen teams reduced the beneficial group from "all" to a smaller subset during follow-up (6 teams versus pretraining). The OPCAB attitude at 3 months ("benefit for all") could be predicted reliably (receiver operating characteristic = 0.92) by variables describing the team and the CMEST variability: the size of the clinic ("number of cases"), the pretraining participation in interactive discussions about OPCAB, the CMEST duration (more than 1 day), the CMEST team membership of an anesthesiologist, and the extent of complexity score reduction (at exit versus pre-CMEST).

The *complexity score* increased slightly at 3 months, versus the exit information, to 1.6 ± 1 ($P <.001$) but was still significantly lower than the complexity score before OPCAB retraining (mean difference: −2.0; $P <.001$). The retraining variability was related to the decrease in complexity score at 3 months: the number of clinical cases participated in during the retraining and the deletion at exit of intraseptal and intramural vessels as OPCAB complexity criteria ($R^2 = 0.66$). The OPCAB complexity variables most frequently cited at 3 months were: intraseptal vessels and intramural vessels. Figure 2 depicts the 10 most frequently cited complexity criteria versus their prevalence before the retraining and at exit. The posterolateral location of coronary anastomoses remained absent from the list.

The OPCAB *application rate* of the surgeons increased about 26% (absolute increase) or 110% (relative increase) 3 months after the OPCAB retraining (49% ± 32% versus 23% ± 28% pre-visit; $P <.0001$). The average OPCAB application rate of the staff surgeons who did not participate in the training did not change during the 3-month interval (8.2% versus 10.3%; $P =.21$).

The increase of the OPCAB application rate after training could be estimated by pre-visit variability; thus, surgeons mainly doing CABG and those who had already attended large audience OPCAB education programs increased their OPCAB rates, whereas surgeons who had been already performing more than 80% of their CABGs off-

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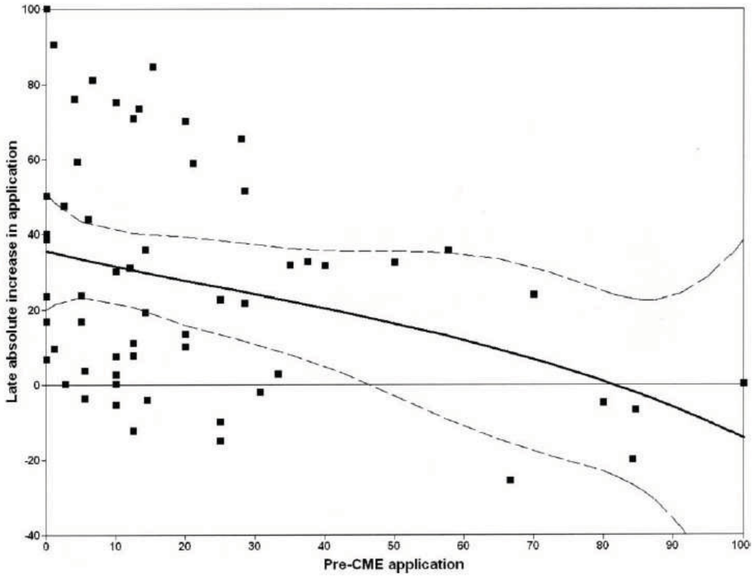

Figure 2. The 3-month increase or decrease in OPCAB application rate, the polynomial transformation and its uncertainty, is plotted versus the pretraining application rate. *CME,* Continuing medical education.

pump did not further increase their OPCAB rates after the training. The pretraining attendance of video-transmitted live demonstrations (unrelated to the educational process studied in this manuscript) had a negative impact on the 3-month OPCAB increase. The predictive model was further improved by a CMEST-associated variable: the deletion of intraseptal coronary location as an OPCAB complexity (Table 2). It turned out that some surgeons with no or very limited OPCAB experience were able to perform nearly all cases off-pump in the weeks after our CMEST. The 3-month increase and decrease of the OPCAB application rate is plotted versus the pretraining application rate (Figure 2). A significant correlation was found between OPCAB attitude at 3 months and OPCAB application ($P <.001$).

The *conversion rate* to CPB improved from 3.5% ± 5% (pre-visit) to 1.3% ± 3% ($P =.006$).

Discussion

Limitations of the Dataset and of the Analysis

The analysis is limited by the size and the variability in the dataset. The team as well as the individualized approach was based on earlier CMEST experience in Leuven (see Methods section), as was the 2-day optimal duration. The analysis was no randomized controlled trial because no visiting team would agree to be the placebo team.

Before one can study the effect of additional variability, one has to build evidence about a basic effect of CMEST. This was missing about OPCAB application and conversion. We have tried to create indirect information about the

TABLE 2. Pretraining and training-associated factors influencing the increase of the OPCAB rate of the surgeons during a 3-month interval after training (multivariate linear regression analysis, $P <.001$, $R^2 = 0.46$)

Variable	Estimate	P value
+ Effect of pre CMEST CABG focus of surgeon (in % of total activity)	76.3	.0062
+ Effect of participation pre CMEST in OPCAB education (large audience)	12.9	.0018
− Effect of pre CMEST OPCAB rate >80%	−22.3	.0057
− Effect of attending pre-CMEST an OPCAB live demonstration	−12.9	.018
− Effect of citing "intraseptal coronary" at exit as a complexity criterion	−6.4	.048

nonvisiting members of a team and have used them as a control group. The analysis includes only 50 teams (70 surgeons), thereby limiting the multivariate correcting capacity.

The reported late application rates were not validated by an independent observer, but there is strong evidence[17] that self-reports of behavior change accurately represent the actual change after CME courses.

Attitude Toward OPCAB

Attitude, a cognitive variable, has been documented[18] to be one of the most important drivers toward change. Self-motivation serves as a driving force to absorb knowledge. Gardner[19] describes 7 important elements influencing the process of change of the individual: reason, research, resonance, representational redescriptions, resources/rewards, real world events, and resistances. Reason or attitude implies that an individual is able to see a logical, rational approach to the pertinent issue and weigh each consideration appropriately. A surgeon would be able, for example, to evaluate each risk and benefit of the OPCAB procedure as it compares with conventional CABG surgery and make an honest assessment as to whether to change his or her belief.

The attitude toward OPCAB in the retrained surgeons was strongly improved by the training as well at exit as at the late evaluation, although somewhat less. The OPCAB attitude at 3 months ("benefit for all") could be predicted reliably, aside through other factors, by training elements (duration of the training more than 1 day, the presence of an anesthesiologist in the team, and extent of complexity score reduction during training).

Complexity Scoring

Complexity scoring is based on cognitive and motor skills, since previous OPCAB experience and exposure will influence this scoring. Surgeons not combining a sling support with an apical suction device and those without OPCAB education experience had more complexity variables at entry.

The scholars were exposed during their training interval to different surgical complexities, addressed as well by the expert as by themselves under the corrective supervision of the expert. Custers and associates[20] and Banderas[21] identified that the effect of this exposure is maintained and even accumulated across repeated exposures, providing observers with opportunities to discern the structure of the modeled actions, to organize and verify what they know, and to give special attention to problematic aspects in subsequent exposures.

The score-reducing effect, at exit, of the training remained stable at 3 months. The posterolateral location of coronary anastomoses disappeared permanently from the list of complexity criteria. The most frequently cited variables at 3 months, intraseptal and intramural coronary anatomy, are already challenging for regular CABG. The prevalence of certain of these complexity criteria in the limited number of attended procedures during the training certainly affected this complexity score. However, surgeons who were not considering an intraseptal coronary as complexity variable for OPCAB at end of the training were more likely to increase their OPCAB rates.

Application and Conversion

The final purpose of a retraining is an improved benefit for the patient. This needs to be preceded by a widened application in the spectrum of patients carrying improvable risk. This study has identified a highly significant increase over a short interval. Nonparticipating surgeons from the same unit did not increase at all (control group), indicative of disappointing absence of knowledge transfer to the colleagues within the unit. Educational material provided was seldom shared within the unit, according to the open questionnaires. The predictive model of the 3-month application rate included characteristic elements of OPCAB retraining (attitude, complexity score). A great variability in training effect was identified. Some surgeons with minimal OPCAB experience before training performed OPCAB in the majority of their patients, a target not reached by 50% of the visiting surgeons.

The appearance of cognitive variables such as attitude and complexity scores in the multivariate model is additional proof of the major importance of cognitive elements in the process of change.

The K.U.Leuven OPCAB retraining model focuses on a team approach. Literature about technology implementation has strongly recommended such an approach when tacit knowledge was deeply imbedded in an interpersonal interaction. This is certainly valid for OPCAB application, where this can improve coordination[22] and reduce complications during the initial experience,[23] and our analysis confirms observations made in unrelated domains. Virtual training models are evaluated in fidelity (similar) to reality (the human heart). Low-fidelity training models are known to be as beneficial[24] to surgical learning as high-fidelity models. Low-fidelity virtual training models are enthusiastically used in the K.U.Leuven resident training and were actively demonstrated to the visiting scholars; only 6 teams actually built such a simple model and practiced with them. This confirms the literature[25] identifying the reluctance of model practicing in surgical trainees. The pretraining experience of a live procedure seemed to have had a lasting negative effect on the posttraining application rate. It is certain that most live procedures fail on aspects of education and technology transfer. The lasting negative effect is dis-

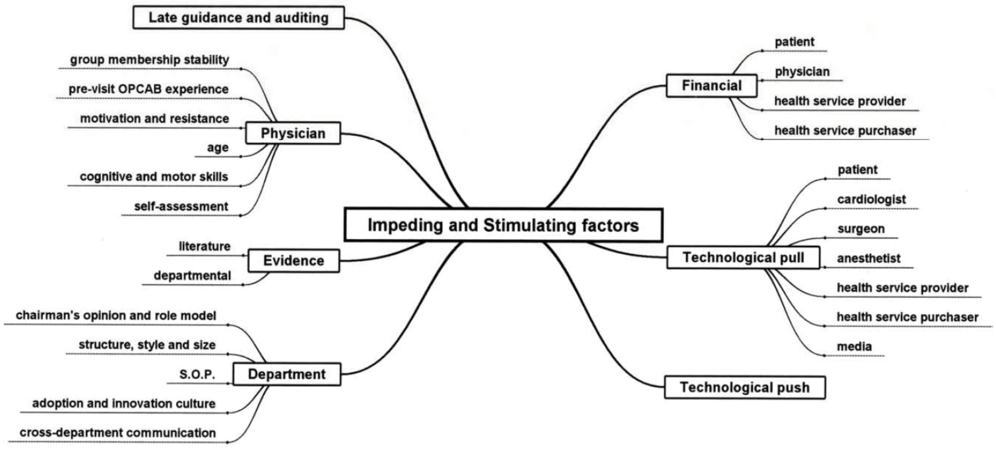

Figure 3. The mind map of the impeding and stimulating factors after retraining. OPCAB, Off-pump coronary artery bypass; S.O.P., standard operating procedure.

turbing and probably needs reconfirmation in additional trials.

Figure 3 structures the most frequently cited impeding and stimulating factors in the application of a new technology, as identified in scientific literature. The size and the specialization of the originating institution determined the complexity score, the OPCAB attitude, and/or the OPCAB application rate. This has been similarly identified in laparoscopic techniques where size of the clinic and the specialization stimulated the adoption.[26,27] The seniority of the visiting teams had no effect on the posttraining application. No correlation of the years since surgical license and the OPCAB application was observed in a study about adoption of OPCAB in Canada.[28] More experienced surgeons should have a greater capacity for knowledge acquisition and integration, but their return to investment decreases with the number of years left in practice.[27] While Desai and colleagues[28] observed a significant correlation between OPCAB attitude and OPCAB application, we found this correlation only after the training rather than before the training. Furthermore, we still recognize in many surgeons the apparent discrepancy between a positive OPCAB attitude and a low application rate. The OPCAB attitude is not the only influencing factor. In addition to the previous mentioned factors, there is also an important role of the departmental chairman, according to our questionnaire, either as a formal opponent (veto in 6 teams) or sometimes as an absence of role modeling. There was no pretraining written commitment of the chairman to implement the technology in his unit after the training, but this might have been a limitation of this CME. The veto of the chairman was the impeding factor in 55% of the nonstarters after a laparoscopic[29] course. The chairman has to provide the psychologic safety[30] in the application of new technologies.

Training Team Stability and Expertise

A possible bias of the late results of this study is the team stability and expertise. The surgical expertise was very variable, often not exceeding the 100 CABG cases a year. This was indicative of smaller cardiac surgery programs, a large number of consultants, or absence of superspecialization in coronary surgery. The superspecialization in cardiac anesthesia was absent in many of our anesthesia scholars, who frequently rotated as a consultant in the different domains of anesthesia. One can expect that these anesthetists would be less familiar with the hemodynamic issues of OPCAB anesthesia. This was insufficiently documented in the pretraining variability. In addition, for departmental reasons, some visiting teams were never allowed to interact in clinical OPCAB cases after their return. A final aspect of the team impact could have been that the entry and exit questionnaires were completed in the presence of the complete team, but this might not have been valid for the 3-month questionnaire.

Conversion Rates

The reduction of the conversion rate concomitant with the increase in application after this multimodal retraining is an identifiable improvement in quality of care. A conversion toward ECC, sometimes as frequent as 13%, has been

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associated with increased mortality[31] and morbidity. Edgerton and coworkers[32] have identified limited experience in OPCAB technique as an important predictor towards conversion.

Conclusion

CMEST is a very intricate process involving an in-depth understanding of the nature of knowledge and the mechanisms of its transfer. An individualized cognitive approach, based on labor-intensive and interactive discussions, team participation, repeated observations, and hands-on practices, can affect the application of a new technology. The impeding effects of institutional variables could be countered by pre-visit discussions about departmental commitments to change. Further analysis is mandatory about improved pre-visit testing and teaching, superior team selection, mandatory written commitment by the chairman, the feasibility and benefit of extending this OPCAB CMEST beyond the 2-day interval, the benefit of a mandatory participation by the chairmen of cardiac surgery and anesthesia, the extended exercise on low-fidelity models, and other possible improvements.

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Appendixes

Appendix 1: Variables of the Entry Form

Unit: Country; type of hospital (academic, non-academic); number of staff surgeons; number of licensed surgeons; number of surgeons with OPCAB experience; annual number of isolated CABG, isolated valves, combined CABG/valves, assist devices, transplants, congenital; number of isolated OPCAB; OPCAB conversion rate; outcome data: stroke rate(overall and high risk), dialysis (overall and high risk), early mortality (hospital and 3 months)

Team: Structure of the visiting team by number of surgeons; anesthetists, and nurses; home interaction of visiting team; experience with modes of OPCAB retraining; expectations; stabiliza-

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tion methods used; shunt use; OPCAB benefit attitude; retraining decision and financing mode; OPCAB complexity score

Each physician: Years licensed; CABG and OPCAB routine

Appendix 2: Variables of the Exit Form

Team: OPCAB benefit attitude; OPCAB complexity score

Retraining activity: Number of days; number of cases attended, observation of conversion (Y/N); team action: deep stitch placement, cardiac manipulation, shunt insertion, low-fidelity training

Appendix 3: Variables of the 3-Month Form

Unit: Number of isolated CABGs of last 3 months; number of isolated OPCABs of last 3 months; OPCAB conversion rate; late evaluation of their educational material

Team: Structure stability of the visiting team; interdepartmental teaching of surgeon, anesthetist, or nurse; stabilization methods used; shunt use; low-fidelity training experience; OPCAB benefit attitude; OPCAB complexity score; open questions about their OPCAB experience

Each physician: CABG and OPCAB routine

5.3.5. Technische Aspekte der T-Graft-Technik: Berechnung der erforderlichen Bypass-Länge mittels einer einfachen Formel (Originalpublikation V)

Albert A, Hassanein W, Florath I, Voehringer L, Abugameh A, Ennker J (2008a). Technical aspects of composite arterial T-grafts: estimation of required conduit length by a simple formula. Thorac Cardiovasc Surg. 56:461-6.

Die Total Arterielle Revaskularisation am schlagenden Herzen wurde entsprechend der in Leuven gelernten Technik im Jahr 2005 bei uns eingeführt und bald als Methode erster Wahl für die koronare Bypassoperation bestimmt. Neben der vollständigen Vermeidung der Aortenmanipulation besitzt sie den Vorteil, dass dabei ausschließlich Aa. Mammariae als Bypassmaterial verwendet und damit die Voraussetzungen für eine optimale Haltbarkeit der Bypässe geschaffen werden. Ein Problem, welches in der Literatur bekannt ist und die Verbreitung der Methode auch in unserer Klinik hemmte, sind Befürchtungen, dass die Länge der als T-Graft in die LIMA inserierte RIMA nicht ausreicht, um alle Bypässe zur Hinter-Seiten-Wand des Herzens bis hin zum RIVP zu legen.

Abgeleitet aus theoretischen Überlegungen entwickelten wir eine einfache Formel zur Berechnung der erforderlichen Länge der RIMA, von der Insertionsstelle in der LIMA (auf Höhe des RIVA) bis zum RIVP. Zur Berechnung der Formel werden die routinemäßig erhobenen echokardiographischen Parameter Wanddicke (WD) und diastolischer Durchmesser des linken Ventrikels (LVEDD) verwendet: 2,14*([2*WD]+LVEDD). Wir testeten diese Formel dann an 100 konsekutiven Patienten, indem wir während der OPCAB-Operation die erforderliche Länge ausmaßen und sie dann mit der für diese aus echokardiographischen Parametern vorhergesagte Länge verglichen. Wir fanden eine hervorragende Korrelation der vorhergesagten mit den beobachteten Werten. Die Formel überschätzte im Durchschnitt leicht (ca. 1cm) die wirklich benötigte Länge und nur in einem Fall mit ausgedehntem Hinterwandinfarkt kam es zur Unterschätzung der Länge. Die Formel hilft Unsicherheit während der Operation zu beseitigen, ausreichende Länge der RIMA zu gewinnen und trägt zur Standardisierung und Training der Methode bei [Albert 2008b]. In der täglichen Praxis kann auch eine vereinfachte Faustformel verwendet werden: 2*LVEDD+4*WD+1

Technical Aspects of Composite Arterial T-Grafts: Estimation of Required Conduit Length by a Simple Formula

Authors A. Albert, W. Hassanein, I. Florath, L. Voehringer, A. Abugameh, J. Ennker

Affiliation Heart Institute Lahr/Baden, Lahr, Germany

Key words
- coronary bypass surgery
- OPCAB
- total arterial revascularisation

Abstract

Background: When composite arterial T-grafts are used, uncertainty persists as to whether the RIMA will be long enough to reach the RCA. We present a formula for the preoperative estimation of the required conduit length.
Methods: The following formula was created to estimate the required conduit length for a sequential graft, starting from the proximal RIMA-LIMA T-graft anastomosis, passing the PLA, and ending at the PDA: 2.14 × ([2 × LV wall thickness [WT]) + end-diastolic diameter (EDD)]. The estimated length was compared to the measured length in 100 patients undergoing off-pump revascularisation with BIMA T-grafts.
Results: There were no hospital deaths, no major infarctions and no wound complications. The required conduit length varied from 11.5 cm to 19 cm (average 14.9 ± 1.4 cm) and was excellently predicted by the formula (paired *t*-test: $p < 0.001$, $r = 0.86$, average overestimation: 0.55 cm).
Conclusion: The formula reliably determines the minimum required conduit length. We recommend this formula for preoperative decision making when considering the choice of graft and the length of RIMA harvesting. To facilitate calculation a simplified version is useful: 2 × EDD + 4 × WD + 1. Avoiding uncertainty about the sufficiency of the RIMA length may contribute to the spread of this technique.

Introduction

In patients with triple vessel disease, CABG exclusively using IMA-T or Y-grafts with multiple sequential side-to-side RIMA-coronary anastomoses has introduced the concept of coronary arterial tree reconstruction by the most appropriate conduit [1]. It capitalises on the expected longevity of this graft. Preferably it is combined with a no-touch aorta off-pump technique, in which any manipulation of the aorta and thus the potential risk of intraoperative embolic events is avoided [2]. Recent studies have confirmed the efficiency of this concept, demonstrating most notably the sufficiency of the flow reserve of the LIMA to supply the entire heart at rest and at stress [3 – 6]. Particular cases have recently been reported, where a reduced patency of sequential grafts due to competitive flow was observed, especially in situations with only moderate stenosis of the posterolateral artery (PLA) or a large dominant right coronary artery (RCA). However the angiographic and clinical relevance of this phenomenon seems to be less important when IMAs and not radial arteries are used for sequential grafting [7,8]. This technique has not been widely adopted yet. A major factor impeding the spread of the technique may be its challenging technical aspects. Accidental stenosis of the IMA T-grafts or of the sequential side-to-side IMA-coronary anastomoses may have serious consequences for the myocardial blood supply. Nevertheless, the incidences of anastomotic stenoses and the rates of perioperative infarction and graft occlusion have been low in the series reported to date [3,6,8 – 10]. Controversy still persists as to whether the RIMA is long enough to reach the RCA, particularly in consideration of the marked individual variations in IMA length and heart size [6,8 – 14]. Surgeons use different strategies to overcome the problem of a short RIMA: use of the *in situ* right gastroepiploic artery [1,11,13, 14], aortocoronary vein grafts [9,11], a radial artery [14], the use of RIMA only for revascularisation of the left ventricle or special techniques of composite arterial grafting such as tangential K or tandem grafts [9,10,15]. However, this may lead to additional complications and involves an

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Correspondence
Dr. Alexander Albert, Consultant
Heart Institute Lahr/Baden
Hohbergweg 2
77933 Lahr
Germany
alexander.albert@heart-lahr.com

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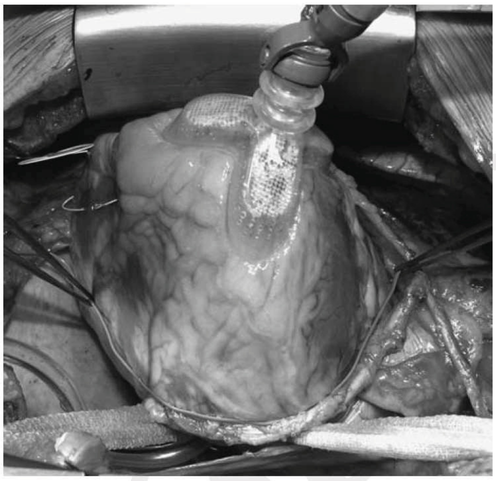

Fig. 1 Intraoperative measurement of the distance from the LAD to the PDA with a measuring tape.

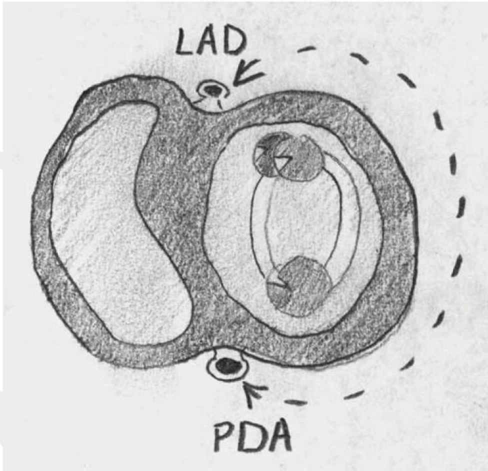

Fig. 2 View of the left ventricle at the level of the papillary muscles. The distance from the LAD to the PDA around the left ventricle can be estimated as circumference of the left ventricle $[(2 \times r) \times \pi = (\text{LVEDD} + 2 \times \text{WT}) \times 3.14]$ minus the anterior-posterior length of the septum (which has approximately the length of the diameter of the ventricle $[(2 \times r) = (\text{LVEDD} + 2 \times \text{WT})]$. LVEDD = left ventricular end diastolic diameter; WT = wall thickness. (Drawing by Victor Gross, Stuttgart, on the basis of a figure by Anderson RH, Kanani M. MMCTS February 19, 2007).

undesirable intraoperative change of strategy, hampering the reproducibility and safety of the technique. In order to optimise and standardise the procedure and to increase its safety, we have introduced into our daily clinical praxis a simple formula based on routine echocardiographic data to estimate the required RIMA length preoperatively. We have tested this formula in a series of patients during off-pump coronary artery bypass grafting (OPCAB), where measurement of the exact length is easier.

Methods

Patients

Between January 1, 2006 and December 31, 2006, 424 patients underwent OPCAB (50% of all CABG patients). All patients gave their informed consent prior to the procedure for the procedure itself as well as for data acquisition and analysis. In order to minimise the selection bias, measurements of required conduit length were performed only in those patients who were operated by the surgeons who performed OPCAB in more than 90% of their CABG patients and who chose IMA-T grafts with multiple sequential side-to-side RIMA-coronary anastomoses as the first choice procedure. A total of 100 patients were enrolled in the study.

Surgical OPCAB technique and measurements of the distance from the LAD to the PDA

OPCAB was performed in an standardised fashion according to the techniques of the Leuven OPCAB school (http://www.opcab-training.eu). The technique as well as the methods and training have been described in detail elsewhere [16,17]: We used some modifications of these techniques with regard to the harvesting of the IMAs (skeletonised IMAs, according to the technique described in [12]), the sequence of grafting (proximal T-graft anastomoses prior to the first distal anastomoses) and the routine use of a blower.

The way in which the heart is enucleated is important for the exact intraoperative measurement of the required conduit length, because during the enucleation process the shape of the ventricle changes. After anterior wall revascularisation the heart was lifted with a sponge sling, fixed at the posterior pericardium in the sinus obliquus pericardii as high and as right-sided as possible. The mass of the LV was placed exactly between the two arms of the sling and the heart was lifted. This makes the shape of the heart become spherical. After rotation of the table, and preload optimisation, an apical suction device (Starfish, Medtronic, Minneapolis, MN, USA) was attached to the anterior wall. Then the left ventricle was gently elongated, thereby changing the shape of the heart from a spherical to an elliptical shape; afterwards the heart was gently displaced towards the right side followed by a readjustment of the pericardial sling to support the heart from below, thereby minimising the risk of mitral insufficiency. Then the distance between the proximal LAD and the proximal PDA was measured manually using a measuring tape (**Fig. 1**).

Formula for the required conduit length

The length required for a sequential graft inserted into the LIMA on the level of the proximal LAD passing the marginal branches of the circumflex artery to reach the proximal PDA, can be estimated by the *circumference* of the LV minus the anterior-posterior length of the septum, septum length is approximately equivalent to the *diameter* of the ventricle (**Fig. 2**). Using to two variables which are easily available with routine echocardiography before surgery, namely, the end-diastolic diameter (EDD) and wall thickness (WT), the diameter of the LV can be calculated as follows: EDD + 2 × (WT). Since the LV has the shape of a circle (in

Table 1 Characteristics of the study patients compared to average CABG patients in Germany. *Annual report of the "Bundesgeschäftsstelle Qualitätssicherung 2004"

Patient characteristics	%/mean of the study population	%/mean of the German CABG population*
Age [years]	67 ± 9	66.9
Male gender	79	77
Body mass index	28 ± 4	28
Body size [cm]	172	170.8
Body weight [kg]	84	81.4
Ejection fraction > 50 [%]	75	74.9
Ejection fraction 30 – 50 [%]	24	19.1
Ejection fraction < 30 [%]	1	6
EuroSCORE	4 ± 2.7	5.8
COPD	17	8
Chronic atrial fibrillation	2	3.6
Compensated renal insufficiency	10	16.2
On dialysis	1	1.1

Table 2 Procedural and outcome data for the 100 study patients

Procedural and outcome parameters	%/mean
3 peripheral anastomoses	54
4 peripheral anastomoses	39
5 peripheral anastomoses	7
Operating time [min]	195 ± 40
Mortality, in-house	0
Mortality, 30 days	0
Perioperative myocardial infarct	5 (no patient with significant reduction of EF)
Max CK-MB during hospital stay [U/l]	average 27.2, median 17.5

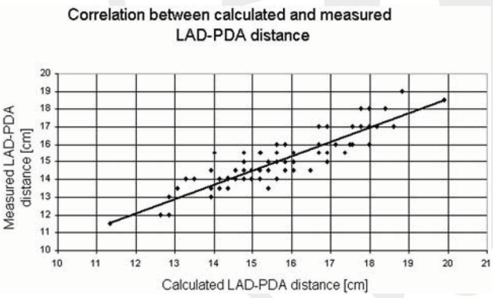

Fig. 3 The correlation between calculated and measured LAD-PDA distance was excellent.

a cross-sectional view) and the LAD and the PDA lay both on the septum, the LAD-PDA distance around the free wall of the LV is calculated as (EDD + 2 × [WT]) × 3.14 – (EDD + 2 × [WT]) = (EDD + 2 × [WT]) × 2.14

Evaluation of the formula and the descriptive statistics was performed with the statistical software JMP Statistics and Graphic Guide, Version 5 (SAS institute Inc., Cary, NC, USA)

Results

100 patients with triple vessel disease were operated by two surgeons (first and last authors). With regard to demographic data, and comorbidities the patients did not differ from patients receiving CABG in Germany (**Table 1**). Patients with severely reduced ejection fraction were underrepresented in our series, since composite arterial grafting and OPCAB are used less frequently in these patients. The short-term outcome was excellent (**Table 2**).

In three patients with a very dominant RCA in addition to the composite grafts with double IMAs an aortocoronary vein graft was anastomosed to the RCA. In five patients the PLA of the RCA was anastomosed, all others received a RIMA composite graft from the LIMA to the PDA. The length of the RIMA free graft would always have been sufficient to reach the PDA. The required conduit length or the measured LAD-PDA distance, respectively, ranged from 11.5 cm to 19 cm (**Fig. 3**, **Table 3**). About 50% of the hearts were of normal size, whereas 30% showed isolated hypertrophy of the myocardium, and the rest had either an isolated dilatation of the LV or a combination of both hypertrophy or dilatation (**Table 4**).

Estimation of the LAD-PDA distance or the required conduit length with the formula was excellent (**Fig. 3**, $p < 0.001$, correlation coefficient 0.86) with an overestimation of 0.55 cm on average (95% CI: 0.4 – 0.7). In 1 patient with a normal sized heart and a large posterior infarction, the formula underestimated the required conduit length by 2 cm.

Discussion

Several studies have shown that in patients with triple vessel disease, composite arterial grafts can be safely performed, with excellent angiographic and clinical results [3 – 5,8,10,18 – 20]. The economic approach for sequential grafting using a RIMA, starting from a T-shaped insertion into the LIMA, using a diamond-shaped side-to-side anastomosis for the posterolateral vessels, and ending with a T-shaped perpendicular end-to-side anastomosis for the PDA, is the preferred method. Nevertheless, technical challenges and pitfalls with this technique have been reported and often concern the issue of length of the sequential graft. Such risks are real: **Table 5** shows the length of the different arterial grafts and how short they can be. Accordingly the preoperative estimation of the required length is a prerequisite for the proper planning of the revascularisation strategy. Performing sequential arterial grafting during cardioplegic arrest has an associated risk of tension between anastomoses after filling the ventricle. It is recommended to make the length of the IMA segment between anastomoses 5 – 10 mm longer than the actual distance between the anastomotic sites in the coronaries [12]. However, a lot of surgical experience is necessary to foresee the ideal length for all anatomic conditions, impeding the adoption of this procedure by others; if the segment between anastomoses is too long, kinking of the RIMA, creating sharply angled curves or twists, jeopardises the patency of the graft. In addition, giving additional length and making curves between the coronaries wastes RIMA length which carries the risk that the graft will be too short to reach the PDA without stretching. Performing sequential grafting on the beating heart is straightforward since measurements of the required conduit length and placement of the anastomoses are made under true conditions with

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Table 3 Distribution of EDD, WT, calculated and measured LAD-PDA distance

Parameters	Mean	Median	25% quart.	75% quart.	Min	Max
LVEDD [cm]	4.8	4.5	4.4	5.4	3.5	6.3
WT [cm]	1.2	1.2	1.2	1.3	0.9	1.8
Calculated LAD-PDA distance [cm]	15.5	15.2	14.3	16.7	11.3	19.9
Measured LAD-PDA distance [cm]	14.9	14.5	14.0	15.5	11.5	19

LVEDD = left ventricular end-diastolic diameter; WT = wall thickness (either septum or posterior wall)

Table 4 LAD-PDA distance in normal, hypertrophic and dilated hearts

	N	Measured length [cm]	Calculated length [cm]	Maximum length [cm]
Normal hearts	53	14.3	14.6	17
Hypertrophy and LV dilatation	7	18.6	17.2	19
Only hypertrophy	32	14.9	15.7	17
Only dilatation	8	17	17.5	18

Table 5 Overview on the length of arterial grafts

Type of graft	Average length [cm]	Minimal length [cm]	Reference
LIMA	20.7[1]	16.2[1]	[22], at autopsy
RIMA	20.1[1]	15.1[1]	[22], at autopsy
Radial artery	20.5	15.2	[24], intraoperatively
IEA	13	8	[23], intraoperatively

[1] Full length measured at autopsy from origin to bifurcation, which is about 2 cm (0.5 cm to 4.4 cm) longer than the harvestable LIMA, corresponding to the crossing of the phrenic nerve. IEA: inferior epigastric artery

normally filled ventricles. However, since arterial grafts have a limited length, depending on the type of graft and the individual anatomy of the patients, there remains the risk that the RIMA will not be long enough for complete revascularisation, impeding the safety and reproducibility of the procedure

The formula introduced here allows the required conduit length to be estimated preoperatively and is based on simple, routinely available echocardiographic data.

The formula excellently predicts the distance between LAD and PDA. In only 1/100 patients did it underestimate the required length; this could have been expected since a large posterior infarction with localised dyskinesia had already been diagnosed preoperatively. Slight to moderate overestimation of the LAD-PDA distance was more common. A cause for overestimation may be that the thickness of the wall was measured only at one point (mostly the posterior wall area). It would be possible to eliminate this inaccuracy by using an average of several wall diameter measurements at different parts of the LV. However, the formula should stay simple and should be based only on values derived from routine echocardiography, which often contain limited information about the thickness of the wall. In daily practice a slight to moderate overestimation is no drawback for the formula, because its main function is to indicate the minimum required conduit length without too much overestimation.

Volume changes of the ventricle obviously had no important impact on the estimation and measurement of conduit length in our study.

Fig. 4 The extra length needed for one deviation can be estimated using Pythagoras' theorem ($a^2 + b^2 = c^2$) = (original length^2 + deviation^2 = c^2): extra length ($c - a$) = $\sqrt{\text{original length}^2 + \text{deviation}^2}$ – original length. The extra length needed for a second deviation (here: d – e) should be added to the first, in order to estimate the total extra length needed (Drawing by Victor Gross, Stuttgart).

In addition to the circumference of the LV, other factors may influence the arrangement of the grafts and the required conduit length. Proximally calcified or small distal coronaries as well as diagonal coronaries originating distal to the proximal LAD-PDA axis are the most frequent reasons requiring the RIMA to deviate from the usual course, necessitating extra length.

The extra length needed for one deviation can be estimated by Pythagoras' theorem: extra length = $\sqrt{\text{original length}^2 + \text{deviation}^2}$ – original length (**Fig. 4**). To simplify this equation, **Fig. 5** shows the extra length needed in various situations. As illustrated in this figure, *one* deviation does not usually need a significant additional length. Nevertheless, when two deviations

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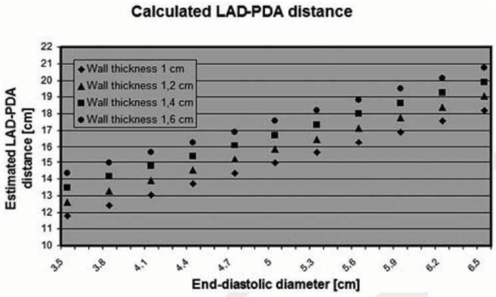

Fig. 5 Calculated LAD-PDA distance depending on different wall thicknesses and left ventricular end-diastolic diameters.

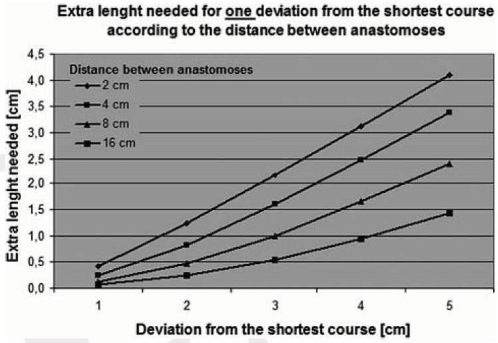

Fig. 6 Estimation of extra length needed for *one* deviation. In the event that the sequential graft (RIMA) forms a curve, 2 deviations are made, resulting in a twofold extra length.

are needed, forming a curve in the RIMA (**Fig. 4**, e.g., proximally calcified obtuse marginal artery combined with a distally non-graftable PDA), up to 25% more length is needed.

To overcome the problems of graft length and course and to find the optimal arrangement it is recommended, before opening any coronary artery on the posterior or lateral wall, to begin by identifying all sites where anastomoses should be done and to plan the graft arrangement. Some surgeons perform the proximal anastomosis only after finishing all the distal anastomoses [16]. Nevertheless, during OPCAB it is very attractive to create the RIMA-LIMA T-graft anastomoses prior to the distal anastomoses and prior to lifting the heart in order to have immediate and definitive myocardial perfusion on completion of every distal anastomosis. In our experience and in that of others [21] the level of the pulmonary valve is always a suitable place for insertion of the T-graft. When a diagonal artery anastomosis is needed, the site of the T-graft may be a little distal, but this deviation from the optimal axis may waste RIMA length. Alternatively the LIMA can be used either sequentially for side-by-side revascularisation of the diagonal or as the safest approach, a second LIMA T-graft to the diagonal is performed using a small end-piece of RIMA or LIMA [6].

Consequently, a thorough study of coronary angiography together with echo data needed to estimate the graft length and a physical examination of the thorax (distance between the sternoclavicular junction and the sixth intercostal space [21,22]) are simple measurements that make it easy to plan a safe and stress-free operation. The surgeon is provided with information about how far he should harvest the RIMA, if necessary beyond the bifurcation. In the rare cases with an expected mismatch between the required conduit length and free RIMA, an alternative conduit should be planned already preoperatively. On the other hand incomplete harvesting of the RIMA is also possible, with the advantage of saving the sternum circulation in its most vulnerable distal part, as recommended in obese and/or diabetic patients [20]. Instead of calculating the estimated length, this may be taken from our chart (**Fig. 6**). In daily practice a simplified version of the formula for quick calculation is useful: $2 \times EDD + 4 \times WT + 1$. We believe that avoiding uncertainty about the sufficiency of the RIMA length and appropriate standardisation may encourage the spread of this technique.

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5.3.6. Analyse des Umstellungsprozesses von konventioneller Bypassoperation zu TOPCAB (Total Arterielle OPCAB) und der Effekte auf Inzidenz und Schweregrad perioperativer Schlaganfälle (Originalpublikation VI).

Albert A, Sergeant P, Florath I, Ismael M, Rosendahl U, Ennker J (2011). A process review of a departmental change from conventional CABG to TOPCAB (Total Arterial OPCAB) and its effect on the incidence and severity of postoperative stroke. Heart Surg Forum 14: 61-68.

In der vorliegenden Arbeit wird in Prozess der Umstellung von konventioneller Bypassoperation zu TOPCAB beschrieben, angefangen bei der Implementierung des neuen Verfahrens durch den Autor im Jahr 2005 in einer herzchirurgischen Klinik bis zur nahezu vollständigen Adaptation von OPCAB durch alle 18 Chirurgen und Assistenten in 2010. Für das Studium einer solchen Entwicklung hatte es sich als hilfreich erwiesen, in Anlehnung an entsprechende Prozessanalysen aus der Industrie, die 4 Phasen der Initiierung, der Implementierung, des Hochfahrens und der Integration zu unterscheiden. Die vorliegende Studie ist damit Bestandteil der Integrationsphase, in der rückschauend das bisher Erreichte umfassend analysiert und bewertet wird.
Der statistische Vergleich zur konventionellen Bypassoperation bezüglich operativer Letalität (Krankenhaus- und 30-Tage-Letalität), und Schlaganfallrate wird mittels logistischer Regression unter Einbeziehung des Propensity Scores durchgeführt. Hier wird nicht zwischen OPCAB und TOPCAB differenziert. Die Darstellung von Lernkurven und die Fehleranalysen werden mit VLADS (siehe Publikation 3) und Einzelfalldiskussionen durchgeführt. Dabei wird beurteilt, inwieweit eine mögliche Vermeidbarkeit von den schweren Komplikationen vorgelegen haben könnte. Stimulierende und hemmende Faktoren werden benannt und dabei auch die Ergebnisse einer Mitarbeiterbefragung und der externen Qualitätssicherung berücksichtigt.
TOPCAB wurde innerhalb von 4 Jahren zuerst durch den Autor und den Chef der Abteilung, dann von den jüngeren Operateuren, später durch die erfahreneren Oberärzte, und letztlich durch die Ausbildungsassistenten übernommen (67% OPCAB). In der Zeit von 2005-2008 wurden 1781 OPCAB- und 1563 ON-PUMP Operationen durchgeführt. Der Unterschied in den Letalitäten zwischen OPCAB und ON-PUMP war nach Risikoadjustierung nicht mehr signifikant (Krankenhaus-/30-Tage-Letalität: OPCAB: 10 (0,6%)/21 (1,2%), ON-PUMP:

27(1,7%),26(1,7%)). Dagegen blieb die um 60% niedrigere Schlaganfallrate auch nach Risikoadjustierung signifikant (0.4% versus 1%, $p<0.05$). In keinem Fall mit Anwendung der aortalen No-Touch-Technik wurde ein früh postoperativer Schlaganfall beobachtet. Lernkurven waren nachweisbar, eine mögliche Vermeidbarkeit des Versterbens lag in 30% aller Fälle vor. Die Einstellung des Teams gegenüber TOPCAB war überwiegend positiv, Gründe dafür waren die sich entwickelnden Routinen, die guten Ergebnisse im Klinik-Ranking und der externen Qualitätssicherung sowie das positive Echo der einweisenden Ärzte. 6 Jahre nach Initiierung des Umstellungsprozesses, werden mehr als 90% der Bypassoperation als TOPCAB durchgeführt.

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Process Review of a Departmental Change from Conventional Coronary Artery Bypass Grafting to Totally Arterial Coronary Artery Bypass and Its Effects on the Incidence and Severity of Postoperative Stroke

Alexander Albert,[1] Paul Sergeant,[2] Ines Florath,[3] Mohammed Ismael,[4] Ulrich Rosendahl,[3] Jürgen Ennker[3]

[1]Department of Cardio-Thoracic Surgery, University Clinic Düsseldorf, Düsseldorf, Germany; [2]Department of Cardiac Surgery, Gasthuis University Hospital, Leuven, Belgium; [3]Department of Cardiac Surgery, Heart Institute Lahr/Baden, Lahr, Germany; [4]Department of Cardiac Surgery, University Clinic, Jena, Germany

ABSTRACT

Background: We evaluated the process of changing from conventional coronary artery bypass grafting (CABG) to totally arterial off-pump coronary artery bypass (TOPCAB) at a single heart center in Germany.

Methods: We (1) used multivariate statistical methods to assess real-time monitoring of OPCAB effects, (2) conducted a case review to assess preventable deaths and identify areas of improvement, (3) conducted a team survey, and (4) evaluated benchmarking results.

Results: All surgeons and assistants (n = 18) at this center were involved and were guided by the department head and one of the consultants, who was trained in this procedure in 2004 at the Leuven OPCAB school. The frequency of OPCAB operations increased abruptly in 2005 from 5% to 43% and then increased gradually to 67% (n = 546) by 2008 (total, 1781 OPCAB cases and 1563 on-pump cases). The in-hospital and 30-day mortality rates for OPCAB surgeries (n = 10 [0.6%] and 21 [1.2%], respectively) were lower than for on-pump surgeries (n = 27 [1.7%] and 26 [1.7%], respectively). Stroke rates were also lower for OPCAB surgeries (7 cases [0.4%] versus 15 cases [1%]). The lower risk of stroke in the OPCAB group was significant ($P < .05$) after risk adjustment. Monitoring curves and case reviews demonstrated a preventable death percentage of at least 30%. The attitude of the team was mostly positive because of the promising results (eg, fewer strokes, increasing TOPCAB popularity, and a top national rank).

Conclusions: The change from conventional CABG to TOPCAB was effective in decreasing the incidence and severity of stroke, in developing a team routine and a positive team attitude, and in producing excellent benchmarking results. The presence of a training and communication deficiency at the beginning of the study suggested an area for further improvement. After 6 years TOPCAB had largely replaced conventional CABG.

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Correspondence: Alexander Albert, MD, Vice Chairman, Department of Cardiovascular Surgery, University of Düsseldorf, Moorenstrasse 5, 40225 Düsseldorf, Germany; +49-0-211-81-18331; fax: +49-0-211-81-18333 (e-mail: alexander.albert@med.uni-duesseldorf.de).

INTRODUCTION

Use of off-pump coronary artery bypass surgery (OPCAB) offers the opportunity to reduce early mortality and the incidence of postoperative stroke [Sergeant 2004]. The use of arterial grafts is known to increase the longevity of bypass grafts compared with the use of venous grafts. Thus, our department in 2005 wanted to shift its strategy from conventional coronary artery bypass grafting (CABG) to totally arterial OPCAB (TOPCAB). The entire team was involved, and the process was guided by the department head and one of the consultants, who was trained in this procedure at the Leuven OPCAB school in 2004. The purpose of this study was to evaluate the new strategy with regard to possible application rates, the different methods of internal quality control, benchmarking data derived from national quality control, and the subjective attitudes of team members. In this report, we describe our use of a process review that allowed us to experience how the difficulties evolved and were eliminated over the various stages of converting to TOPCAB. These stages were initiation, implementation, ramp-up, and, finally, integration [Szulanski 2000].

MATERIALS AND METHODS

OPCAB Strategies

The data set includes 3344 patients with coronary artery disease who underwent either CABG procedures with extracorporeal circulation (n = 1563) or OPCAB procedures (n = 1781) at the Heart Institute Lahr/Baden between March 2005 and December 2008. OPCAB (primarily TOPCAB) became the procedure of choice for the department head and the retrained consultant, and it represented 90% of all CABG procedures during this time. At the same time, a number of the surgeons in the team were put on a schedule of a gradual learning curve (ie, expanding the

Table 1. Selection of Preoperative, Procedure-Related, and Outcome Data*

Variables	Entire Group	OPCAB Group	On-Pump Group	*P*
Preoperative data				
Age, y	66.8 ± 9.6	66.5 ± 9.7	67.3 ± 9.5	.013
Female sex, %	25.3	23.1	27.8	.001
Insulin-dependent diabetes, %	13.1	21.1	14.1	NS
Carotid stenosis, %	20.3	20.1	20.6	NS
History of stroke, %	10.1	10.3	10.0	NS
Dialysis, %	0.9	1.0	0.8	NS
EuroSCORE (additive)	4.5 ± 3.0	4.2 ± 2.9	5.0 ± 3.1	<.001
Ejection fraction, %	59 ± 28	59 ± 14	59 ± 38	NS
Hyperthyroidism, %	6.9	7.2	6.6	NS
Hypothyroidism, %	4.6	5.4	3.8	.02
Leukocyte count, $\times 10^9$/L	8.0 ± 5.5	7.95 ± 6.7	7.98 ± 3.7	NS
Operative data				
Emergency cases, %	4.1	2.0	6.5	<.001
Multivessel disease, %	91.1	88.6	94.0	<.001
No. of anastomoses	3.0 ± 1.0	2.9 ± 0.97	3.1 ± 0.92	<.001
Use of bilateral IMAs, %	45.6	56.6	33.1	<.001
Operation time, min	188 ± 52	185 ± 50	191 ± 54	.001
Postoperative data				
Arrhythmias, %	33.7	31.3	36.5	.001
Psychosyndrome, %	4.0	2.9	5.3	.001
Infarct, %	1.8	1.7	1.9	NS
CKMB maximum, U/L	44 ± 72	33 ± 54	57 ± 87	NS
Dialysis, %	4.5	4.0	5.1	NS
In-hospital mortality, %	1.1	0.6	1.7	.001
30-Day mortality, %	1.4	1.2	1.7	NS
Strokes (including RINDs), %	0.7	0.4	1.0	.04
Strokes (excluding RINDs), %	0.5	0.2	1.0	.002

*Data are presented as the mean ± SD where indicated. OPCAB indicates off-pump coronary artery bypass; NS, not statistically significant; IMA, internal mammary artery; CKMB, creatine kinase isoenzyme MB; RIND, reversible ischemic neurologic defect.

surgeon-technique spectrum) [Song 2003]. Thus, the propensity toward the OPCAB approach was clearly a biased one. Finally, the strategy of the surgical team was to use bilateral internal mammary arteries (IMAs) in performing OPCAB surgery and to use composite arterial grafting (ie, TOPCAB). Patients in a critical preoperative state (as defined by the EuroSCORE) and redo CABG procedures were excluded from the study.

Surgical Technique

OPCAB was performed in a standardized fashion according to the techniques of the Leuven OPCAB school ([Albert 2006; Peck 2007], http://www.opcab-training.eu). The key feature of this technique is the division of the OPCAB procedure into distinct components from the surgical and anesthesiologic procedural points of view. The routine use of a pericardial sling and an apical suction device for positioning and the use intracoronary shunts play a major role. Automated ST-segment analysis, readings of central venous and pulmonary artery pressures, and intermittent cardiac output measurements (Swan-Ganz catheter) are used for hemodynamic monitoring. We applied modifications of the Leuven TOPCAB techniques in different aspects of the procedure. These aspects included IMA harvesting (use of skeletonized IMAs), the grafting sequence (use of proximal T-graft anastomoses before the first distal anastomoses) [Albert 2008], use of a blower, and routine use of flow measurements for all CABG procedures. On the other hand, the on-pump CABG approach included the use of blood cardioplegia and a single-clamp technique.

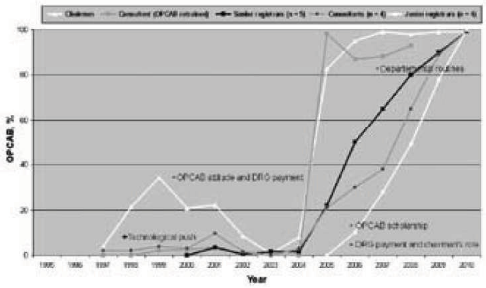

Figure 1. Departmental rates of off-pump coronary artery bypass (OPCAB) application according to professional group. The major stimulating (+) and restraining factors (-) for implementation of the new technology are shown. Data from 2009 and 2010 are included in this figure. DRG indicates diagnosis-related group.

Internal Quality Control

Data Set. For each patient included in the presented study, 49 preoperative characteristics were used from the consolidated database of our data mart system [Arnrich 2004]. The data were based on the anesthesiologic and cardiosurgical quality-assurance data and clinical chemistry laboratory data. Table 1 summarizes the data set. All variables included in the analysis had a missing-data rate of <5%. For missing values, we used the mean for continuous variables and the most frequent event for categorical variables.

Follow-up. Mortality within 30 days was assessed meticulously (data >99% complete) by means of a specific procedure that we have performed routinely since 1996. This procedure is based on questionnaires and phone calls to the patients after discharge. Patients with any neurologic dysfunction before and after surgery underwent routine evaluations by neurologists. These evaluations included brain computed tomography scans and have been described previously [Albert 2003].

Real-Time Monitoring. For real-time monitoring of in-hospital mortality, we created online variable life-adjusted displays (VLADs) based on a database updated daily, as described previously [Albert 2004]. Multiple VLAD types may thus be selected according to type of procedure, individual surgeon, or time period.

Multiple Regression Models. To adjust for confounding variables, we estimated the impact of OPCAB on in-hospital mortality by logistic regression analysis. Statistical analysis was performed with the SPSS software package (SPSS, Chicago, IL, USA). For the selection of variables, we minimized the Akaike information criterion. To further account for imbalances in the distribution of risk factors between patients who underwent OPCAB or the on-pump technique, we calculated a saturated propensity score by logistic regression, irrespective of the factors' significance levels. We then calculated the propensity score for every patient and forced it into the model.

Case Conferences. We conducted routine case conferences to evaluate all adverse events. During these meetings we also performed chart reviews to determine the preventability of adverse events. This evaluation was carried out by identifying problems with processes of care and then judging whether these problems contributed to the poor outcome. On the basis of these results, we rated preventability retrospectively by increasing strength of preventability ("none," "slight," "modest," "strong," and "certain"). This evaluation was carried out according to a previously described method [Guru 2008], and areas of improvement were discussed.

External Quality Control

The data of the Deutsche Gesellschaft für Thorax-, Herz-, und Gefäßchirurgie (DGTHG) (http://www.dgthg.de) and the national quality assessment by the BQS Institute (http://www.bqs-outcome.de) provide comparisons of hospital-specific data and national averages with respect to case mixes, performed procedures, and risk-adjusted mortalities (all annual reports since 1995 are published on the MediClin Herzzentrum Lahr/Baden Web site (http://www.mediclin.de/herzzentrum-lahr/desktopdefault.aspx) at BQS/AQUA-Bundesauswertung and Jahresberichte under the Qualität tab.

Surveys of Team Attitudes

We enrolled 38 team members in the study from January to February 2008 (18 surgeons, 8 anesthesiologists, 3 physicians from the intensive care unit, and 9 scrub nurses). Data were collected via questionnaires. The collected data included current and previous attitudes regarding OPCAB benefits, technical issues, and proposals for improvement. Additional questions assessed the subjective evaluation of OPCAB results (mortality, stroke, myocardial infarction, graft occlusion, bleeding, and wound infections) and patients' and cardiologists' attitudes toward OPCAB.

RESULTS

Application Rates

The rate of OPCAB application in the department increased abruptly from 5% (n = 41) in 2004 to 43% (n = 371) in 2005 and increased progressively thereafter until 2008, when the rate was 67% (n = 546). The cumulative total was 1781 cases (Figure 1). The rate of use of both IMAs increased concurrently. Approximately 60% of OPCAB procedures involved the use of bilateral IMAs (TOPCAB), whereas use of bilateral IMAs occurred in only 35% of on-pump cases. Table 1 compares procedure-rated data for OPCAB and on-pump surgeries.

Internal Quality Control

Case Conference of OPCAB Patients. Of 11 OPCAB patients who died in the hospital, 6 were obviously high-risk patients (emergencies, critical preoperative state, ejection fraction <30%, age >80 years). Another 10 OPCAB patients died after discharge but within 30 days. Seven of the OPCAB patients developed a stroke, and the occurrence of stroke was delayed in all patients but one, who had undergone partial clamping of the aorta (Table 2). Residual symptoms of

Table 2. Patients Who Developed a Focal Neurologic Deficit during Their Hospital Stay*

Patient No.	Year	Clinic	Onset	Localization	Residuals	Partial Clamping	Age, y	Risk Factors
1	2005	Stroke	Delayed	Internal capsule	Slight	No	83	History of stroke
2	2005	Stroke	Delayed	Brain stem	Slight	No	73	Aortic atheromatosis (grade V, Turnik classification)
3	2006	RIND	Delayed	Unclear	No	No	73	Postoperative AF
4	2007	RIND	Delayed	Posterior cerebral artery	No	No	80	Postoperative AF
5	2007	Stroke	Delayed	Multiple infarcts	Severe	No	82	Postoperative AF, left carotid artery occlusion, right carotid artery stenosis, left vertebral artery occlusion
6	2008	RIND	Delayed	Left hemisphere	Slight	No	75	Postoperative AF
7	2008	RIND	Early	Thalamic syndrome	No	Yes	73	No

*RIND indicates reversible ischemic neurologic defect; AF, atrial fibrillation.

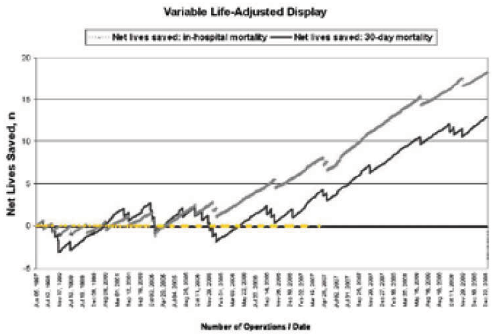

Figure 2. Multiple variable life-adjusted display (VLAD) charts, which was created automatically and updated daily by input from our database [Albert 2004]. OPCAB performance data since 1995 are illustrated. The number of operations is indicated by the thickness of the small yellow bars on the x-axis. To estimate the death rate within 30 days, we derived the items and additive weights from the simple EuroSCORE to calculate the expected mortality (EM) for our patients [Roques 1999]. For all patients the EM was in the range of 0.002 to 0.1. VLADs were created by continuous display of operative results. In the case of a successful operation, the curve goes up by the EM value for this patient; if the patient dies, the curve decreases by the value of 1 EM. If the patient was at a high risk of perioperative death, the surgeon's mortality figures are not unduly penalized, but mortality figures are penalized when a low-risk patient dies. The cumulative results for every patient display the overall performance. The expected cumulative mortality minus the actual cumulative mortality is the net lives saved.

reversible ischemic neurologic defects (RINDs) after discharge were severe in 1 patient, slight in 3 patients, and absent in 3 patients.

Online Monitoring of Surgical Performance (VLADs). Both VLAD curves indicated positive OPCAB performance, compared with both the internal references and the EuroSCORE reference (Figure 2). Obviously, an accumulation of unfavorable events occurred in the years before the change process, as well as during 2005.

Risk-Adjusted Effect of OPCAB on Mortality. The in-hospital and 30-day mortalities were 11 patients (0.6%) and 21 patients (1.2%), respectively, for the OPCAB group. The corresponding mortalities for the on-pump group were 27 patients (1.7%) and 26 patients (1.7%). The risk-adjusted difference in in-hospital mortality and 30-day mortality for the OPCAB approach was not significant after correcting for propensity and event-related variation.

Risk-Adjusted Effect of OPCAB on Stroke. The incidence of stroke before discharge was 7 patients (0.4%) for the OPCAB group and 15 patients (1%) for the on-pump group. The 60% non–risk-adjusted difference in prevalence with the OPCAB approach was significant in the univariate analysis, but this difference lost statistical significance after correction for propensity and event-related variation (see Model 1 in Table 3: c index, 0.818; chi-square, 12.886; P = .117, Hosmer-Lemeshow test). When the RIND cases were excluded, the difference between the OPCAB and on-pump groups (0.2% versus 1.0%) remained significant in the multivariate analysis (see Model 2 in Table 3: c index, 0.84; chi-square, 15.559; P = .049, Hosmer-Lemeshow test).

External Quality Control

Application Rates of OPCAB (Annual Reports of the DGTHG). The number of OPCAB procedures performed in Germany did not change significantly from 2005 to 2008 (5264, 5199, 5036, and 5362 cases, respectively). The proportion of OPCAB cases increased only slightly during this period, from 9.7% to 10%. A few departments (18, 17, 13, and 14 departments for the years 2005 to 2008, respectively) performed >100 OPCAB procedures per year. Since 2005, our department performed the highest numbers of such procedures in Germany (2005, 371 cases; 2006, 426 cases; 2007, 438 cases; 2008, 546 cases).

Rates of Totally Arterial Revascularization. The use of bilateral IMAs for complete revascularization more than doubled, from 20% in 2005 to 47% in 2008. TOPCAB was used in 58% of the patients (some surgeons used this technique for >90% of their patients). In Germany, the percentages of CABG procedures with 2 arterial grafts were 16.8% in 2008 and 18.3% in 2007.

Table 3. Effect of Off-Pump Coronary Artery Bypass (OPCAB) on All Strokes and on Complete Strokes Only with Residuals after Discharge (Excluding Reversible Ischemic Neurologic Defects)*

	Model 1: All Strokes		Model 2: Complete Strokes Only	
Variable	Estimate	P	Estimate	P
Saturated propensity score	−3.859	.01	−4.815	.003
Noncardiac comorbidity				
Higher WBC	1.20	.007	1.124	.023
Peripheral artery disease	1.662	.001	1.730	.001
History of stroke	2.074	.001	2.088	<.001
OPCAB effect	−0.552	.257	−1.346	.040

*Multivariate regression analysis; c index values are 0.81 and 0.84 for models 1 and 2, respectively. WBC indicates white blood cell count.

Hospital Comparison of Non–Risk-Adjusted and Risk-Adjusted In-Hospital and 30-Day Mortality. Table 4 summarizes the annual outcome data for all CABG procedures (including reoperations) in our department, compared with the national averages. The department ranked second, third, fourth, or fifth (national CABG ranking by the BQS Institute) in the years 2005 to 2007 (http://www.mediclin.de/herzzentrum-lahr/desktopdefault.aspx; see under Qualität tab). The 2008 rankings were the worst because of the worse results for the on-pump group (the in-hospital mortality rate for elective OPCAB patients was 0%; the 30-day mortality rate was 3 of 546 patients, 0.6%).

Surveys of Staff Attitude. Eighty-five percent of the team members considered OPCAB beneficial for all patients, 73% of the team members anticipated a reduction in the incidence of postoperative stroke, and 41% anticipated a reduction in postoperative mortality. Attitudes toward the OPCAB technique differed among the different groups of hospital staff (Figure 3).

All of the physicians, however, considered the technological pull (patient demand) for this newly introduced technique to be a positive factor in stimulating the use of OPCAB (78% of anesthesiologists, 93% of surgeons, and 75% of intensivists). The majority of the surgeons and intensivists noticed the bias of the referring physicians toward OPCAB and the TOPCAB technique.

The scrub nurses complained predominantly that OPCAB is time-consuming (100%) and that there were noticeable individual differences between surgeons in performing OPCAB surgery. They argued for a more competent selection of the surgical team (67%). Anesthesiologists, surgeons, and scrub nurses believed the incidence of hemodynamic instability during the procedure to be approximately 50%, 15%, and 40%, respectively (P = .004). Fifty-eight percent of the anesthesiologists believed that hemodynamic instability is a major problem of this procedure; however, none of the surgeons believed this.

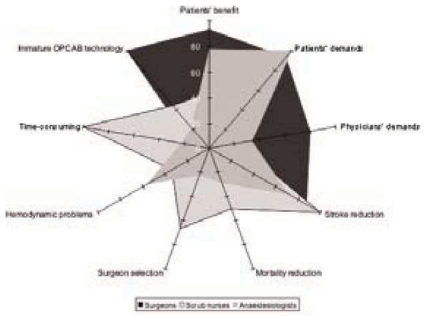

Figure 3. Survey of staff attitudes.

DISCUSSION

Aproximately 6 years passed before conventional CABG was largely replaced by the new TOPCAB technique. Various factors stimulated the implementation process: (1) It was initiated by a modification in the national diagnosis-related group (DRG) payment system in 2005 that abolished any difference in reimbursement between on-pump and OPCAB procedures (see "payment system" [Banta 1993]). (2) The department head made an explicit commitment to move the department toward performing TOPCAB procedures. This decision was based on his perception of the relative advantages of the procedure and therefore of a need to have superior expertise in this technique to compete with other surgical centers (see "competition" [Poulsen 1998]). (3) The 1-year fellowship at the Leuven OPCAB school for the retrained consultant provided the required information, technical skills, enthusiasm, belief, and strong motivation to endorse TOPCAB as a set technique for all CABG patients (see "Leuven OPCAB school" [Albert 2006] and "surgical training" [Wanzel 2002]).

The retrained consultant implemented the Leuven OPCAB technique overnight in the new environment as the procedure of first choice. The consultant provided evidence that the knowledge to be transferred was robust and that the source was reputable [Szulanski 2000]. The prompt adoption of this technique by the head of the department, established that this standardized procedure is teachable. The continuous 1-year intensive training program for the retrained consultant produced a more stable process of knowledge transfer than, for example, the 3-day Leuven OPCAB courses [Albert 2006]. The intensive training provided the opportunity for deliberate practice, facilitated expert feedback [Wanzel 2002], and led to a more stable process of knowledge transfer, all of which were due to the experiences shared with the Leuven OPCAB team (see "shared experience" [Nonaka 1994]).

The role of the department head was of utmost importance, not only during the initiation and implementation stages but also during the ramping-up stage. He provided psychological support and safety, which facilitated a healthy learning environment [Edmondson 1999]. Additional factors that

Table 4. Risk-Adjusted (Logistic EuroSCORE) Comparison of Mortalities in Heart Institute Lahr/Baden versus the National Average*

Year	In-Hospital Mortality			30-Day Mortality†		
	Dead/Total, n	O/E Lahr versus National Average	Rank	Dead/Total, n	O/E Lahr versus National Average	Rank
2005	13/819	0.23 versus 0.51	3	18/819	0.31 versus 0.53	4
2006‡	8/689	0.19 versus 0.52	2	12/689	0.28 versus 0.57	3
2007	7/797	0.08 versus 0.40	2	11/795	0.12 versus 0.45	4
2008§	17/841	0.21 versus 0.41	8	22/840	0.27 versus 0.42	22

*See http://www.bqs-outcome.de and http://www.mediclin.de/herzzentrum-lahr/desktopdefault.aspx (see under Qualität tab). O indicates observed mortality; E, expected mortality (by logistic EuroSCORE).

†Follow-up rates at Heart Institute Lahr/Baden were 100% (2005), 100% (2006), 99.7% (2007), and 99.9% (2008). National average follow-up rates were 72.14% (2005), 75.21% (2006), and 72.9% (2007).

‡In 2006, all EuroSCORE variables were exported for only 689 of 806 patients because of a change in the hospital information system.

§Only 2 of the 17 in-hospital deaths and 3 of the 22 deaths occurring within 30 days were in the off-pump coronary artery bypass group. The other deaths were for conventional coronary artery bypass grafting (CABG) or redo CABG operations.

allowed an optimal climate for the positive diffusion of the newly implemented technique [Poulsen 1998; Albert 2006] were the following: the rich database; the closed recording and different measures of internal quality control, including online monitoring of surgical performance [Albert 2004; Arnrich 2004]; various debriefing activities; data transparency and the positive benchmarking results (see "debriefing activities" [March 1975]), which enhanced team attitudes toward OPCAB (see "attitude" [Dirksen 1996]); the competitive attitude of the working team; specialization (in the cardiac field); and the adequate existing collection of surgical skills. Our plan involved including all coronary patients, without exclusion, because shifting back and forth between conventional and OPCAB techniques increases the challenges to participants because of the risk of not developing habitual routines [Hackman 1990].

In contrast, the factors that restrained TOPCAB implementation were the high number of surgeons and trainees who had different OPCAB attitudes and skills and who had been performing CABG procedures routinely. Furthermore, the different interests of the various consultants and the different heart surgery specialties led to a lack of interest and a reluctance to change [Albert 2006]. Therefore, a number of the surgeons in the team were placed on a schedule that involved a gradual learning curve (ie, expanding the surgeon-technique spectrum [Song 2003]).

The procedure is now fully institutionalized. This stage of integration is characterized by a progressive development of routine, which is incipient in every recurring social pattern. With respect to the complex interaction between performance improvements and future adoption, there may be virtuous and vicious cycles at work. Early adoption of the technique and initial successes may lead to an interest in performing more cases. This positive feedback leads to a growing volume of cases, which in turn may stimulate further performance improvements. The commitment of the recipient to specific practices will become evident during the integration stage, because each time complications occur, the appropriateness of the new practice can be explicitly questioned [Szulanski 2000].

According to the present study, the most important effect of TOPCAB implementation (beside the significant increase in arterial revascularization) has been a significant reduction in the incidence and severity of stroke. In the multivariate analysis, a preference for OPCAB with respect to the occurrence of stroke and RINDs was not identifiable; however, the subgroup analysis (only strokes with residuals) suggested a significant preference. Of note is that we had a limited ability to prove some of the crucial points of debate because of a lack of statistical power, low event rates, selection bias, a short observation period, and problems with subgroup analysis. We conclude from our data that TOPCAB leads to a relevant decrease in the incidence and severity of postoperative stroke. The results in the literature regarding the neurologic benefit of the OPCAB procedure vary [Raja 2005]. In our experience, the necessary preconditions for achieving an OPCAB benefit are (1) elimination of the risk of intraoperative embolism by avoiding any manipulation of the aorta and (2) application of appropriate OPCAB techniques by a well-trained team to ensure hemodynamic stability during the entire procedure. Noteworthy is that all but one the stroke patients in our series emerged from their operations without focal neurologic deficits. This patient was one of a very few patients who had undergone partial clamping for a proximal anastomosis. This finding suggests that avoiding partial clamping during the OPCAB procedure produces better results and abolishes the iatrogenic trigger for the occurrence of a neurologic deficit [Lev-Ran 2005]. Most obviously, postoperative de novo atrial fibrillation was the cause of delayed strokes in the OPCAB patients.

An OPCAB benefit with respect to in-hospital or 30-day mortality was not evident after risk adjustment. First, the analysis was not statistically powered to identify a mortality difference for these periods of time. Second, although the risk profile of the OPCAB sample (mean ± SD, 4.1% ± 0.1%) exceeds the risk profile of the EuroSCORE data set (mean, 3.3% ± 2%), it was still less than that of the on-pump group (mean, 4.9% ± 0.1%). This selection bias has probably decreased the possibility to detect significant differences. Third, by using only 30 days instead of a longer observation interval, we may have missed events that could have affected statistical accuracy. In our experience with CABG follow-up between 2000 and 2004, we identified an additional 30% of the events by extending the follow-up from 30 days to 3 months (1.4% versus 2.1%, unpublished data). Fourth and most importantly, the deficit in outcomes due to learning effects is included in the analysis. An accumulation of unfavorable events in 2005 was detected by the use of VLADs, which indicated preventable deaths.

In this process of drastic change, it is mandatory from the very beginning to closely follow up the possible causes of preventable death and their effects on the statistical outcome of this experience and to try to eradicate the causative factors. Preventable deaths are more likely to be identified for patients with a low operative risk (according to a heuristic understanding of risk [Guru 2008]. High-risk patients, however, are particularly susceptible to problems with the OPCAB procedure, such as periods of low output or low systemic pressure). In our study, 4 (36%) of the 11 in-hospital deaths were judged to have been preventable ("strong" or "certain"). This percentage is similar that of a previous multicenter study [Guru 2008]. In another 6 high-risk patients, we encountered a "slight" or "modest" preventability. In contrast to the preliminary OPCAB experience (before 2004), when the OPCAB technique itself was deficient [Albert 2004; Hassanein 2005], we have now identified other areas for improvement, including intraoperative communication problems, quality assurance, and retraining. One in-hospital death was "certainly" preventable. In this operation, the OPCAB procedure was converted to an on-pump procedure too late in the procedure, and a prolonged situation of low cardiac output caused multiorgan failure. In this case, 2 problems were identified as areas for improvement—insufficient OPCAB retraining (hence indicating conversion) and inadequate communication between the surgeons and anesthesiologists (hence delaying conversion). Such communication problems were also involved in 2 other "slightly" or "modestly" preventable deaths. The surgeon and the anesthesiologist have different points of view with respect to patient management. The anesthesiologist ("accommodator") maintains the patient's hemodynamics under operative conditions, which requires immediate and flexible reactions to encountered acute problems. The surgeon, on the other hand, performs an operation with a specific technical procedure in mind, much as engineers use patterns or blueprints [Baker 1985]. Human cognitive tunnels could be the reason for the differences in the views of surgeons and anesthesiologists toward an operation; such cognitive tunnels are probably important human behavioral risk factors [de Leval 2000].

The views of the different professional groups involved could be seen vividly in our attitude survey. The surgeons focused on the minute technical details (intracoronary shunt placement) and ignored the time factor and hemodynamic instability. The anesthesiologists, however, tended to be alarmed by a patient's instability and the nurses' lack of interest and continuous criticism. A trial to minimize the communication problem would be to set a fixed team. Such a program would facilitate the building of mutual trust among members and would accelerate the creation of an implicit common perspective by the members because of shared tacit knowledge [Nonaka 1994; Edmondson 2003]. Some of the anesthesiologists and the majority of the scrub nurses emphasized the need for surgeon selection for OPCAB. Indeed, surgeon retraining in OPCAB procedures was identified as an improvement area in the preventable death.

CONCLUSION

The different methods of assessing this process of change varied during the different stages of the changeover to OPCAB, and they were either active or passive. These methods were also the initiating and motivating factors that permitted the existence and continuation of this live process. This change involving the application of routines and standardization, which an entire department experienced over a period of time, facilitated optimization and the perfection of performance. Could this technique be the method to achieve the goal of the zero strokes in bypass surgery? We are convinced that if there is any way to avoid stroke totally during the surgical approach to myocardial revascularization, this method would probably be the way.

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6. ZUSAMMENFASSUNG

Prävention neurologischer Komplikationen in der Herzchirurgie

Die hier vorgestellten Untersuchungen führten zu neuen Erkenntnissen über Risikofaktoren und Vermeidungsstrategien des postoperativen Schlaganfalls. Daraus ergaben sich neue präventiven Maßnahmen, deren erfolgreiche Umsetzung in die klinische Praxis zu einer Reduktion der Inzidenz des herzchirurgischen Schlaganfalls führte.

Bereits *präoperativ*, im Rahmen der Operationsvorbereitung, können Risiken des perioperativen Schlaganfalls vermieden werden. Ausgehend von unserer Beobachtung, dass das Schlaganfallrisiko mit Höhe der Leukozytenwerte im Blut korreliert, ergab sich die Empfehlung, Patienten mit erhöhten Leukozytenwerten, wenn möglich, erst dann zu operieren, wenn der zugrundeliegende Infekt behandelt wurde und sich die Leukozytenwerte normalisiert haben. [Selim 2007]. In Tabelle 5 sind die wichtigsten Empfehlungen zur *präoperativen Prävention* des herzchirurgischen Schlaganfalls aufgelistet.

Maßnahmen zur präoperativen Prävention	*Empfehlungsgrad*
Vermeidung eines Blutzuckerwertes > 140 mg/dl (7.8 mmol/l)	Class I (Level A)
Sicherstellung eines Cardiac Index > 2.5 l/min	Class IIb (Level C)
Vermeidung einer Leukozytose	Class IIb (Level C)
Vermeidung von langanhaltenden Blutdruckabfällen >20% oder 20mmHg zu individuellen Normalwerten	Class IIb (Level C)
Karotis-TEA präoperativ oder simultan bei schlecht kollateralisierten hochgradigen A. karotis Stenosen	Class IIb (Level C)
Aussetzen einer elektiven Herz-OP für 6 Monate bei präoperativer TIA	Class IIb (Level B)

Tabelle 5. Maßnahmen zur präoperativen Prophylaxe des herzchirurgischen Schlaganfalls [nach Selim 2007, Djaiani 2006, Grogan 2008, Albert 2003]

Intraoperative Maßnahmen zielen in erster Linie auf eine Vermeidung von Mikro- und Makroembolien sowie von Hypotonien ab.

Wir konnten zeigen, dass die Form der Aortenkanüle mit der Inzidenz und Lokalisation des Schlaganfalls korreliert. Damit ergaben sich neue Hinweise auf die Bedeutung des Sandstrahleffektes bzw. des Venturi-Effektes für das Auftreten von Schlaganfällen, der sich später durch direkte echokardiographische Untersuchungen bestätigte. Als praktische Konsequenz lässt sich ableiten, dass das Embolie-Risiko gesenkt werden kann, indem die Aortenkanüle immer parallel zum Aortenbogen ausgerichtet wird.
Zusammenfassend sind in Tabelle 6 die wichtigsten Empfehlungen zur intraoperativen Prävention neurologischer Komplikationen aufgelistet:

Maßnahmen zur intraoperativen Prävention	*Empfehlungsgrad*
Membranoxygenator und ein arterieller Filter (≤40µm).	Class I (Level A)
Epiaortaler Ultraschall zur Detektion nicht palpierbarer Plaques	Class I (Level B)
Epiaortaler Ultraschall zur Verminderung zerebraler Embolien	Class IIb (Level C)
Kontrolle des Jetstreams der Aortenkanüle	Class IIb (Level C)
Routinemäßige Verwendung der „Single clamp Technik“	Class IIa (Level B)
α-stat pH Management an der HLM.	Class IIa (Level A)
NIRS (Near Infrarot Spectrometry) bei Hochrisikopatienten	Class IIb (Level B)
Arterieller Blutdruck >70 mmHg an der HLM in Risikopatienten	Class IIb (Level B)
Serum-Glucose < 140 mg/dl (7.8mmol/l)	Class IIb (Level C)
Gabe von Erythrozytenkonzentraten bei einem HB-Wert ≤7g/dL bei Risikopatienten und in Abhängigkeit von Begleitumständen .	Class IIb (Level C)

Tabelle 6: Maßnahmen zur intraoperativen Prophylaxe des herzchirurgischen Schlaganfalls [nach Selim 2007, Djaiani 2006, Grogan 2008, Albert 2002]

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Wir beobachteten in der Klinik über die Jahre einen deutlichen Rückgang der Inzidenz postoperativer Schlaganfälle, der sich am ehesten durch die konsequente Anwendung der genannten prä- und intraoperativen Maßnahmen erreicht wurde. Die Inzidenz betrug nun in unserer Studie bei der Bypass- und Herzklappenoperationen ca. 1%. Es konnte gezeigt werden, dass bei der isolierten Bypassoperation eine weitere Reduzierung der Inzidenz um 60% auf 0.4% möglich ist, wenn gleichzeitig auf die Anwendung der Herz-Lungen-Maschine und auf jegliche Manipulation an der Aorta verzichtet wird; bei Betrachtung nur der „completed strokes“ sinken die Inzidenzen auf 0.2%; darüber hinaus kam es durch die Technik des „Anaortic OPCAB“ zu einer Anihilierung des unmittelbar postoperativ auftretenden Schlaganfalls. Ein Vergleich mit den wenigen bisher existieren Serien des Anaortic OPCAB zeigt übereinstimmend, dass die Inzidenz des Schlaganfalls auf deutlich unter 1% gesenkt werden kann. [Tabelle 7, siehe auch Misfeld 2011].

Land	***N***	***%***	***CI***	***Ref.***
Switzerland	271	0,8	0,1-2,5	Emmert 2011
Israel	429	0,2	0,01-1,38	Lev-Ran 2005
US	476	0,8	0,22-2,04	Kapentanakis 2004
UK	226	0,5	0,09-1,7	Patel 2002
Australia	1201	0,25	0-0,56	Vallely 2008
Germany	1550	0,2	0,04-0,56	Albert 2011*

Tabelle 7: Inzidenz des postoperativen Schlaganfalls bei „Anaortic OPCAB“; * Subgruppenanalyse der Anaortic OPCAB aus [Albert 2011].

Wir haben dargestellt, dass der Prozess von der Initiierung eines Veränderungsprozesses durch Einführung von TOPCAB bis zur Integration des neuen Verfahrens in die klinische Routine kompliziert ist und der Berücksichtigung vieler Faktoren bedarf, um für Patienten ungünstige Lernkurven zu vermeiden und die Chancen des Verfahrens zu verwirklichen. Als stimulierende Faktoren der Entwicklung erwiesen sich eine Nutzung verschiedener Modalitäten des Trainings durch entsprechende Experten, die Aufstellung und Befolgung von SOPs, die Anwendung und Förderung des Verfahrens durch den Abteilungsleiter, das zeitnahe Monitoring der Ergebnisse durch ein Online-Berichtswesen, die Nutzung der

externen Qualitätssicherung als Erfolgskontrolle, Ergebnis-Transparenz und Förderung der Team-Motivation.
Bemerkenswert in unserer Serie war, dass keiner der 1550 Patienten, die eine Bypassoperation in der Anaortic OPCAB-Technik erhielten, mit einem neurologischen Defizit aus der Operation erwachten. So bleibt nur das Restrisiko, einen verzögert im Intervall von wenigen Tagen nach der Bypassoperation auftretenden Schlaganfall zu erleiden. Ziel ist es herauszufinden, ob sich durch weitere prophylaktische Maßnahmen, wie beispielsweise eine Intensivierung der Antikoagulation oder Plättchenhemmung, Frühmobilisation oder die systematische Ligatur des linken Herzohrs während der Operation, das Risiko neurologischer Komplikation noch weiter reduzieren oder sogar gänzlich vermeiden lässt.

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