

Almanah 2012.: kardijalna kirurgija odraslih. Časopisi nacionalnih društava predstavljaju odabrana istraživanja koja donose napredak u kliničkoj kardiologiji

Almanac 2012: adult cardiac surgery. The national society journals present selected research that has driven recent advances in clinical cardiology

Ben Bridgewater*

UHSM, Manchester, Velika Britanija
UHSM, Manchester, United Kingdom

SAŽETAK: U ovom preglednom članku obrađujemo važne publikacije iz područja kardijalne kirurgije odraslih objavljene u zadnjih nekoliko godina, uključujući i trenutne dokaze o kirurškoj revaskularizaciji i primjeni kirurgije bez uporabe stroja za izvantjelesni krvotok, lijevoj i desnoj unutarnjoj grudnoj arteriji te endoskopskoj metodi vađenja vene. Promjene tradicionalne kirurgije aortne valvule su opisane zajedno s ishodima kliničkih ispitivanja i registrima za transkatetersku implantaciju aortne valvule te uvođenjem manje invazivnih i novih pristupa tradicionalne kirurgije zamjene aortne valvule. Kirurgija bolesti mitralne valvule se također razmatra uz poseban osvrt na kirurgiju asimptomatske degenerativne mitralne regurgitacije.

Uvod

Kardijalna kirurgija ostaje najvažniji izbor liječenja za mnoge bolesnike sa koronarnom bolesti srca (KBS), bolestima srčanih zalistaka i zatajivanjem srca. Operacija koronarnih arterija je i dalje najčešća operacija koja se provodi u većini centara, ali se njezina učestalost smanjuje u Velikoj Britaniji.¹ Većina bolesnika se podvrgava operacijama mitralnog i aortnog zalistka tradicionalnim i novim pristupima uključujući manje rezove kod tradicionalne kirurgije i umetanje nove proteze koristeći uređaje na bazi katetera. U ovom članku

SUMMARY: This review covers the important publications in adult cardiac surgery in the last few years, including the current evidence base for surgical revascularisation and the use of off-pump surgery, bilateral internal mammary arteries and endoscopic vein harvesting. The changes in conventional aortic valve surgery are described alongside the outcomes of clinical trials and registries for transcatheter aortic valve implantation, and the introduction of less invasive and novel approaches of conventional aortic valve replacement surgery. Surgery for mitral valve disease is also considered, with particular reference to surgery for asymptomatic degenerative mitral regurgitation.

CITATION: *Cardiol Croat.* 2013;8(1-2):56-66.

Introduction

Cardiac surgery remains an important treatment option for many patients with coronary artery disease, valvular heart disease and heart failure. Coronary artery remains the commonest operation undertaken in most centres, but its proportion is decreasing in the UK.¹ More patients are undergoing mitral and aortic valve procedures, both by conventional and novel approaches including smaller incisions for conventional surgery and insertion of new prostheses using catheter-based devices. This article will summarise publications from

Acknowledgement: The article was first published in *Heart* (Bridgewater B. Almanac 2012—adult cardiac surgery: the national society journals present selected research that has driven recent advances in clinical cardiology. *Heart.* 2012;98(19):1412-7. doi: 10.1136/heartjnl-2011-301539.) and is republished with permission.

ćemo prikazati sažetak novijih publikacija koje imaju utjecaj na postupke u području kardijalne kirurgije.

Operacija koronarnih arterija

Vremenom su se uočile značajne promjene kod bolesnika koji dolaze na operaciju koronarnih arterija koje se jasno prikazuju u američkim i britanskim analizama istraživanja velikih serija operiranih bolesnika. Izvješće iz baze podataka Društva torakalnih kirurga (STS databaza) opisuje sve veći rizični profil bolesnika koji dolaze na operaciju — manji broj pušača, više dijabetičara i sve veću primjenu lijeve unutarnje grudne arterije (LIMA) kao prenosnice. Registriran je značajan pad postoperativne smrtnosti i pobola.² O sličnim trendovima je izviješteno iz nacionalne baze podataka kardijalne kirurgije odraslih iz Velike Britanije gdje se od 2000. godine registriira za više od 50% smanjenje rizika smrtnosti, uz već spomenuti rizičniji profil bolesnika i sve češću primjenu unutarnje grudne arterije.^{1,3} No, usprkos dokazima o učinkovitosti, operacije bez uporabe stroja za izvantjelesni krvotok uz višestruke arterijske presadke se nisu počele široko koristiti (vidi niže).¹

Operacija koronarnih arterija ili perkutana koronarna intervencija kod angine

Najveće suvremeno randomizirano kliničko istraživanje za donošenje odluke kod bolesnika sa višezilnom KBS je SYNTAX istraživanje. U studiji je randomizirano 1.800 bolesnika s prethodno liječenom trožilnom KBS i/ili bolešću lijeve glavne koronarne arterije na 85 lokacija u 17 država diljem Europe i SAD. Rezultati jednogodišnjeg praćenja su objavljeni 2009. i pokazuju da je skupina s perkutanom koronarnom intervencijom (PCI) imala višu učestalost zajedničkog ishodišnog cilja od velikih neželjenih kardiovaskularnih ili cerebrovaskularnih događaja i nije uspjela postići prethodno zadani krajnji ishod neinferiornosti.⁴ Ova razlika je registrirana zbog više učestalosti ponovljene revaskularizacije kod skupine liječene primjenom PCI (13,5% za PCI; 5,9% za aortokoronarno premoštenje, CABG). U prvoj godini nisu registrirane razlike u učestalosti smrtnosti ili infarkta miokarda (MI) između dvije skupine pacijenata. Ove razlike postoje tijekom dužeg razdoblja praćenja uz trogodišnje učestalost MACCE (učestalost velikih neželjenih kardiovaskularnih i cerebrovaskularnih događaja; moždani udar, MI ili ponovljena revaskularizacija) koje su više kod skupine liječene primjenom PCI (28%) nego kod skupine liječene CABG (20%), ponovno uglavnom zbog ponovljene revaskularizacije, a nije bila registrirana razlika u primarnom sigurnosnom ishodu ili pojavi moždanog udara. U analizi podskupina nije bilo razlike u velikim neželjenim događajima kod bolesnika sa stenozom glavnog stabla lijeve koronarne arterije (LMS), no ishodi su lošiji nakon PCI u podskupini bolesnika sa trožilnom KBS.⁵ Analiza ishoda temeljena na riziku postupka prema rezultatima Syntax ljestvice je utvrdila da se u razdoblju od 4 godine krivulje razilaze, ali ne i kod bolesnika s niskim stupnjem rizika (<http://www.syntaxscore.com>).

U skladu s rezultatima studije SYNTAX, veliko američko istraživanje podataka iz registara povezano je nacionalni kardiovaskularni registar (ACCF) i bazu podataka kardiovaskularne kirurgije za odrasle (STS) s registrima Medicare i Medicaid, da bi se utvrdili bolesnici sa 65 ili više godina koji su bili liječeni primjenom PCI i CABG. Četiri godine nakon zahvata uočena je dobrobit na preživljavanje u skupini liječenoj primjenom CABG, koja je postojala i u važnim podskupinama.⁶

I dok su kasniji rezultati kod većine visokorizičnih bolesnika s višezilnom KBS bili bolji nakon CABG, u obje studije, ran-

cent years that are having an impact on the practice of cardiac surgery.

Coronary artery surgery

There are marked changes in patients coming to coronary artery surgery over time that have been shown clearly from the analyses of large series from the USA and UK. A report from the Society for Thoracic Surgeons (STS) database has described the increasing risk profile of patients coming to surgery with fewer smokers, more patients with diabetes and more use of the left internal mammary artery (LIMA) as a bypass conduit. Overall, there has been a significant decline in postoperative mortality and morbidity.² Similar trends have been reported in the UK from the national adult cardiac surgery database, where there has been a greater than 50% reduction in risk adjusted mortality since 2000, again with increasing risk profiles, and more use of the internal mammary artery.^{1,3} However, despite some evidence for their efficacy, off-pump surgery and multiple arterial grafts have not become widespread (see below).¹

Coronary artery surgery or PCI for angina

The major contemporary randomised clinical trial to inform decision making in patients with multivessel coronary artery disease is the Synergy between PCI with Taxus and Cardiac Surgery (SYNTAX) trial. The study randomised 1,800 patients with previously treated three vessel or left main coronary artery disease or both in 85 sites in 17 countries across Europe and the USA. The 1-year results were published in 2009, showing that the percutaneous coronary intervention (PCI) group had higher rates of the combined end point of major adverse cardiac or cerebrovascular events and failed to achieve the predefined end point of non-inferiority.⁴ This difference was driven by a high rate of repeat revascularisation in the PCI group (13.5% PCI, 5.9% coronary artery bypass grafting (CABG)). The 1-year rates of death or myocardial infarction (MI) were not different between the groups. These differences persist over longer follow-up with 3-year MACCE rates (death stroke, MI or repeat revascularisation) being higher in the PCI group (28%) than the CABG group (20%), again driven mainly by repeat revascularisation, but there was no difference in the primary safety end point or the incidence of stroke. On subgroup analysis, there was no difference in major adverse events in the patients with left main stem (LMS) stenosis, but outcomes were worse following PCI in the three vessel subgroup.⁵ Analysis of outcomes based on procedural risk from the syntax score has shown at 4 years that the curves are diverging overall, but with no difference in the low risk patients (<http://www.syntaxscore.com>).

In line with the data from SYNTAX, a large registry-based study from the USA linked the ACCF National Cardiovascular registry and the STS adult cardiac surgery database to the Medicare and Medicaid registries and used propensity scoring to match patients who were 65 years or older undergoing PCI and CABG. Four years after intervention there was a mortality advantage in the CABG group, which persisted in the important subgroups.⁶

While the late outcomes of most higher risk patients with multivessel coronary artery disease seem to be better with CABG, in both randomised and registry-based studies, the

domiziranoj i onoj temeljenoj na registru, rezultati nakon intervencije radi LMS nisu bili tako uvjerljivi, posebno u ranoj fazi praćenja. U meta-analizi 2.905 bolesnika s nezaštićenom LMS iz osam kliničkih studija, nije bilo značajnije razlike između skupina u preživljavanju ili zajedničkom ishodu ukupne smrtnosti, MI ili moždanog udara tijekom jedne godine.⁷ Druga meta-analiza 3.773 bolesnika koja analizira trogodišnje razdoblje praćenja donijela je slične rezultate.⁸ Analiza skupine sa LMS iz studije SYNTAX također nije utvrdila razliku tijekom praćenja do 3 godine.^{5,9} Nedavno provedeno istraživanje *Premier of Randomised Comparison of Bypass Surgery Versus Angioplasty using Sirolimus-Eluting Stent in Patients with Coronary Artery Disease* donijelo je rezultate od 300 bolesnika u svakoj podskupini tijekom dvogodišnjeg razdoblja praćenja te je pokazalo da PCI intervencija nije inferiorna metoda liječenja u odnosu na CABG, ali autori su prihvatili široku granicu neinferiornosti te postoji potreba za daljnjim istraživanjima.¹⁰ Slični rezultati dobiveni su također u manjoj studiji.¹¹ Za bolje razumijevanje sigurnosti i učinkovitosti primjene PCI u bolesnika sa LMS i vrijednostima prema Syntax ljestvici ≤ 32 , u tijeku je istraživanje *Evaluation of Xience Prime versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularisation*.^{12,13}

ESC/EACTS smjernice za revaskularizaciju

Europsko kardiološko društvo (ESC) i Europsko udruženje za kardiotorakalnu kirurgiju (EACTS) objavili su u 2010. smjernice za revaskularizaciju koje je načinila uravnotežena ekipa stručnjaka sastavljena od intervencijskih kardiologa, neintervencijskih kardiologa i kirurga. Smjernice savjetuju donošenje odluka od strane odgovarajućeg tima "stručnjaka za srce" sugerirajući da je kirurški zahvat bolji izbor za revaskularizaciju većine anatomskih oblika KBS.¹⁴ Podaci koji su objavljeni nakon izdavanja smjernica uključujući naknadnu analizu istraživanja SYNTAX, dodatno su ojačali dokaze na kojima su utemeljene smjernice. Objavljene su i potencijalne posljedice tih preporuka,^{15,16} no još nisu dostupne detaljne analize bilo kakvih promjena u praksi.

Je li revaskularizacija miokarda bez uporabe stroja za izvantjelesni krvotok sigurna?

Kontraverze oko relativnih prednosti revaskularizacije miokarda sa ili bez uporabe stroja za izvantjelesni krvotok prisutne su i dalje.^{17,18} U Ujedinjenom Kraljevstvu oko 20% zahvata obavljeno je bez primjene stroja za izvantjelesni krvotok, ali postoje proturječni podaci o sigurnosti i dugoročnim posljedicama.¹

Zabrinutost je porasla nakon objave studije ROOBY u kojem je 2.203 bolesnika podvrgnutih CABG randomizirano zahvatu sa ili bez uporabe stroja za izvantjelesni krvotok. Nije bilo značajne razlike u pogledu smrtnosti nakon 30 dana, ali je u skupini kojoj je zahvat obavljen bez uporabe stroja za izvantjelesni krvotok bio veći udio bolesnika koji su prihvatili manje aortokoronarnih prenosnica nego je bilo planirano. Zabrinjavajuća je znatno lošija razlika jednogodišnjeg zajedničkog ishoda od ukupne smrtnosti, ponovljene revaskularizacije ili nefatalnog MI te slabija prohodnost arterijskih prenosnica kod skupine kojoj je zahvat obavljen bez primjene stroja za izvantjelesni krvotok.¹⁹ Kritičari studije su komentirali da je istraživanje uključilo niskorizične muškarce koji bi s najmanjom vjerojatnosti imali koristi od izbjegavanja izvantjelesnog krvotoka, da su kirurzi bili neiskusni i da je bila visoka (12%) učestalost intraoperativne konverzije uz uporabu stroja za izvantjelesni krvotok.²⁰ Osim toga, endoskopska metoda vađenja vene je bila povezana s lošijim ishodi-

outcome following intervention for LMS stenosis is not so clear cut, certainly during early follow-up. In a meta-analysis of patients with unprotected LMS stenosis analysing 2,905 patients from eight clinical studies, there was no significant difference between the two groups with respect to mortality or a composite end point of death, MI or stroke at 1 year.⁷ Another meta-analysis of 3773 patients looking out to 3 years gave similar findings.⁸ Analysis of the left main subgroup of the SYNTAX study also showed no difference up to 3 years.^{5,9} More recently, the Premier of Randomised Comparison of Bypass Surgery Versus Angioplasty using Sirolimus-Eluting Stent in Patients with Coronary Artery Disease trial has reported results of 300 patients in each arm to 2 years, and showed PCI to be non-inferior, but the authors accept that the non-inferiority margin was wide, leaving open the need for further studies.¹⁰ Similar findings have also been detected in a smaller study.¹¹ To understand better the safety and efficacy of the place of PCI for LMS stenosis, the Evaluation of Xience Prime versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularisation trial is ongoing in patients with LMS disease and syntax scores of ≤ 32 .^{12,13}

ESC/EACTS revascularisation guidelines

The European Society for Cardiology and European Association of Cardiothoracic Surgery published guidelines for revascularisation in 2010 that were developed by a balanced writing team of interventional cardiologists, non-interventional cardiologists and surgeons. The guidelines recommend decision making through an appropriately configured 'heart team' and suggest that surgery is the better option for revascularisation for the majority of anatomical forms of coronary artery disease.¹⁴ Data published since the guidelines were released, including later analyses of the SYNTAX trial, have further reinforced the evidence on which the guidelines were based. Potential implications of these recommendations have been reported,^{15,16} but detailed analyses of any changes in practice are not yet available.

Is off pump coronary artery surgery safe?

Controversy remains surrounding the relative benefits of undertaking coronary artery surgery with or without the cardiopulmonary bypass machine.^{17,18} In the UK, around 20% of cases are undertaken off pump but there are conflicting data about safety and longer-term outcomes.¹

Concern was raised from the ROOBY trial in which 2,203 patients undergoing CABG were randomised to surgery on or off pump. There was no significant difference in 30-day mortality, but there were a higher proportion of patients receiving fewer grafts than planned in the off-pump group. Of concern, there was a significantly worse 1-year composite end point of death, repeat revascularisation or non-fatal MI and poorer graft patency in the off-pump group.¹⁹ Critics of the study have commented that the trial enrolled low risk, male patients who would be the least likely to benefit from avoiding cardiopulmonary bypass, the surgeons were inexperienced and there was a high (12%) rate of intraoperative conversion to bypass surgery.²⁰ Furthermore, endoscopic vein harvesting was associated with worse outcomes at 1 year in the study (see further below).²¹ In addition, Moller et al have reported randomised trial data on 341 high risk (EuroSCORE >5) patients with three vessel disease undergoing surgery on or off pump in the Best Bypass Surgery

ma nakon jednogodišnjeg praćenja (vidi u nastavku).²¹ Povrh toga, *Moller i sur* su u istraživanju *Best Bypass Surgery* objavilo randomizirane rezultate istraživanja kod 341 visokorizičnog (EuroSCORE >5) bolesnika s trožilnom KBS podvrgnutom operaciji sa ili bez uporabe stroja za izvantjelesni krvotok. Tijekom prosječnog praćenja od 3,7 godina nije bilo značajne razlike u primarnom ishodu neželjenih srčanih i cerebrovaskularnih događaja, ali je ukupna smrtnost bila veća kod skupine bolesnika operirane bez stroja za izvantjelesni krvotok.²²

Više ohrabrujući podaci nedavno su objavljeni u *MASS 3* istraživanju koje je bilo provedeno u jednoj ustanovi, a koje tijekom petogodišnjeg praćenja između skupina bolesnika nije utvrdilo razliku u zajedničkom ishodu od smrti, MI ili ponovljene revaskularizacije. Također se u *CORONARY* studiji gdje je randomizirano 4.752 bolesnika na zahvat sa ili bez uporabe stroja za izvantjelesni krvotok utvrdilo da među skupinama nema značajne razlike u 30-dnevnoj smrtnosti ili učestalosti MI, moždanog udara ili zatajivanja bubrega.^{23,24} Sa zanimanjem se iščekuju kasniji rezultati ove studije.

Također postoji i meta-analiza 35 studija s uključenih 123.137 bolesnika operiranih s ili bez uporabe stroja za izvantjelesni krvotok. Ona sugerira na superiornost operacije bez uporabe stroja za izvantjelesni krvotok u pogledu kratkoročne smrtnosti i ostalih ishoda.²⁵ U studiji provedenoj u jednoj ustanovi kod 14.766 bolesnika koju su objavili *Puskas i sur* nije bilo razlike u operativnoj smrtnosti kod bolesnika u najnižoj rizičnoj kvartili, dok je registrirana dobrobit kod skupine visokorizičnih bolesnika, što podržava argumente koje su koristili kritičari rezultata studije *ROOBY*.²⁶ Slični rezultati registrirani su kod 349 preživjela bolesnika iz dvije randomizirane studije koje su usporedile operacije sa i bez korištenja stroja za izvantjelesni krvotok, u kojima je kod 199 bolesnika kontrolirana prohodnost arterijskih premošnica i kod 299 bolesnika kvaliteta života, a nije bila registrirana razlika između skupina u razdoblju praćenja 6-8 godina.²⁷

Sve dok su nejasne prednosti ili nedostaci operacije bez uporabe stroja za izvantjelesni krvotok, ostaje interes za optimizaciju ishoda operacije primjenom stroja za izvantjelesni krvotok kroz poboljšanje revaskularizacijskih tehnika. Nedavno istraživanje je privuklo pažnju na činjenicu kako je moguće zaštititi mozak pomoću minimalnog izvantjelesnog krvotoka.²⁸ U toj randomiziranoj usporedbi minimalnog u odnosu na tradicionalni izvantjelesni krvotok, minimalni krvotok je bio povezan s poboljšanom cerebralnom perfuzijom tijekom kardiopulmonalnog premoštenja i poboljšanim neurokognitivnim funkcijama pri izravnom ispitivanju prilikom otpusta, s dokazima o trajnim učincima u razdoblju od 3 i 14 mjeseci. Podaci ukazuju na to da je neke od prednosti koje zagovaraju entuzijasti neuporabe stroja za izvantjelesni krvotok, a posebno cerebralnu zaštitu, moguće postići modifikacijom uporabe stroja za izvantjelesni krvotok.

Je li endoskopska metoda vađenja vene sigurna?

U skladu s drugim pomacima prema manje invazivnim kirurškim tehnikama došlo je do značajnog pomaka prema vađenju vene safene magne kroz minimalno invazivne pristupe uključujući endoskopiju, ali je ostala zabrinutost u vezi sigurnosti takvog pristupa. Kao što je prethodno opisano, podskupina analiza *ROOBY* istraživanja je sugerirala da je endoskopska metoda vađenja vena vezana uz lošije ishode.²¹ Sekundarna analiza bolesnika iz *PREVENT IV* studije nakon trogodišnjeg praćenja rezultata također je pokazala lošije ishode za bolesnike koji su bili podvrgnuti endoskopskom vađenju, ali ti rezultati nisu potvrđeni u drugim opservacijskim studijama.²⁹⁻³¹

trial. There was no significant difference in primary outcome of adverse cardiac and cerebrovascular events during a median follow-up of 3.7 years, although all cause mortality was higher in the off-pump group.²²

More reassuring data have recently been published from the *MASS 3* trial with 5-year follow-up from a single centre with no difference in a composite end point of death, MI or further revascularisation between the groups and from the *CORONARY* study, which randomised 4,752 patients to on or off pump and showed no significant difference in 30-day mortality or the incidence of MI, stroke and renal failure.^{23,24} Later outcomes data from this study are awaited with interest.

There has also been a meta-analysis of 35 propensity score studies on 123,137 patients undergoing on or off pump surgery. This suggested that off-pump surgery was superior for short-term mortality and other outcomes.²⁵ In a single centre study of 14,766 patients reported by *Puskas et al* there was no difference in operative mortality in the lowest risk quartile but increasing benefit for higher risk patients, which supports the argument used by critics of the findings of the *ROOBY* study.²⁶ Similar findings have been reported on 349 survivors of two randomised studies comparing on and off pump surgery in which 199 patients had graft patency assessed, and in 299 patients health-related quality of life, with no difference seen between the groups at 6-8 years.²⁷

While the benefits or otherwise of off-pump surgery are not yet clearly defined, there remains interest in optimising outcomes from on-pump surgery by refining bypass techniques. For example, a recent trial has drawn attention to how the brain might be protected by using a minimal extracorporeal circulation.²⁸ In this randomised comparison of minimal versus conventional extracorporeal circulation, the minimal circuit was associated with improved cerebral perfusion during cardiopulmonary bypass and improved neurocognitive performance on direct testing at discharge, with evidence of sustained effects at 3 and 14 months. The data suggest that some of the advantages proposed by off-pump enthusiasts, particularly cerebral protection, might be achieved by modifying on-pump strategies.

Is endoscopic vein harvesting safe?

In line with other moves towards less invasive surgery, there has been a significant move towards harvesting the long saphenous vein through minimally invasive, including endoscopic, approaches but there remains some concern over safety. As described previously, a subgroup analysis of the *ROOBY* trial suggested that endoscopic vein harvesting was associated with worse outcomes.²¹ A secondary analysis of patients from the *PREVENT IV* trial at 3 years of follow-up also showed worse outcomes for patients undergoing endoscopic harvesting, but this finding has not been confirmed in other observational studies.²⁹⁻³¹

Should bilateral internal mammary artery grafts be used for coronary artery surgery?

It is generally accepted that using the *LIMA* graft to the left anterior descending coronary artery is associated with better inhospital mortality, long-term survival and freedom from angina, and a number of observers suggest that if one mammary is good, two would be better. Despite this, <10% of

Trebaju li se presadci lijeve i desne unutarnje grudne arterije koristiti za aortokoronarno premoštenje?

Općenito je prihvaćeno da je uporaba presatka lijeve unutarnje grudne arterije (LIMA) za lijevu prednju silaznu koronarnu arteriju povezano s boljim bolničkim preživljavanjem, dugoročnim preživljavanjem i uklanjanjem anginoznih tegoba, a mnogi istraživači ukazuju da ako je jedna grudna arterija uspostavila dobru funkciju s dvije će biti još bolje. Unatoč tome <10% aortokoronarnih operacija u Ujedinjenom Kraljevstvu koristi obje unutarnje grudne arterije.¹ Da bi to ispitala, velika randomizirana studija ART je objavila jednogodišnje podatke kod 1.554 bolesnika s ugrađenim jednim LIMA presatkom i 1.548 bolesnika s ugrađenom lijevom i desnom unutarnjom grudnom arterijom (BIMA). To je potkrijepljeno praćenjem 10-godišnjeg preživljavanja. Jednogodišnji podaci pokazuju da između skupina nema razlike u smrtnosti, ali je u BIMA skupini trostruko povećana učestalost rekonstrukcije sternalne rane.³² S obzirom na naša saznanja o vremenu neuspjeha presađivanja vene, bilo bi iznenađujuće u ovom stadiju uočiti bilo kakve prednosti BIMA premoštenja. Daljnji dokaz koji potkrijepljuje koristan učinak BIMA metode prikazan je od studije provedene u jednom centru u kojoj je usporedbom 928 BIMA bolesnika naspram 928 bolesnika s LIMA i presadcima vene safene uočeno produljenje života od 10% tijekom 10-godišnjeg i 18% tijekom 15-godišnjeg razdoblja.³³

Postojalo je veliko zanimanje da se pri operaciji aortokoronarnog premoštenja koristi radijalna arterija, s preporukama od strane entuzijasta da se za poboljšanje dugoročnog ishoda koristi bilo uz obje unutarnje grudne arterije kod totalnog arterijskog premoštenja ili kao dodatak ugradnji jedne unutarnje grudne arterije. Međutim, randomizirana studija sa 733 bolesnika koje je usporedila presadke radijalnih arterija i vena safena nedavno je pokazala sličnu prohodnost presadaka u 1 godini (u oba slučaja 89%).³⁴ U toj studiji zabrinjava povezanost primjene radijalne arterije s povećanom učestalošću vazopazma, dok je korištenje vene safene imalo bolje ishode kod dijabetičara. Zabrinutost je pojačana studijom u kojoj je korišteno CT oslikavanje za ocjenu prohodnosti presadka.³⁵ Međutim, postoji mnogo izvješća koja potvrđuju dobru stopu kasne prohodnosti.³⁶⁻³⁸

Većina studija koja promatra komparativne ishode različitih kirurških pristupa se oslanja na kasne ishode s naglaskom na smrtnost, a takve podatke je očito teško prikupiti te oni donose samo korisne informacije više godina "nakon događaja". Da bi došli do korisnih i pravovremenih različitih podataka, neki istraživači su u potrazi za tehnikama koje daju prednost procjeni preoperativnog rizika ispred kliničkih ishoda zahvata, kao što je operativna ozljeda miokarda lijevog ventrikula. To nije jednostavno kvantificirati i bilo je predmet nedavne studije s Oxforda gdje je 40 bolesnika podvrgnuto oslikavanju kardiološkim MR prije i nakon CABG sa serijskim određivanjem vrijednosti troponina I (TnI).³⁹ TnI je bio usko povezan s masom nove srčane nekroze detektirane oslikavanjem MR ($r = 0,83$, $p < 0,001$), uz osjetljivost i specifičnost od 75% i 87% što predstavlja čvrste pokazatelje dijagnoze ove vrste MI.

Osim analize načina optimizacije operativne kirurške strategije također se sve veća pažnja posvećuje postoperativnim ishodima preživljavanja i tijeku oporavka. Studija objavljena u časopisu Heart ispitala je implikacije postoperativne anemije u retrospektivnoj analizi 2.553 bolesnika iz studije IMAGINE koji su liječeni CABG revaskularizacijom.⁴⁰ Analize su utvrdile da je postoperativna anemija u trajanju >50 dana povezana s većom učestalošću kardiovaskularnih događaja tijekom prva 3 mjeseca. Istraživači su također utvrdili da primjena ACE inhibitora usporava oporavak od postoperativne anemije i povećava učestalost kardiovaskularnih događaja

coronary artery operations in the UK receive both internal mammary arteries.¹ To address this, the ART trial is a large randomised study, which has now reported 1-year data on 1,554 patients receiving a single LIMA graft and 1,548 receiving bilateral mammary arteries (BIMA). It has been powered to look at survival at 10 years. The 1-year data show no mortality difference between the groups but there was a three times increase in the rate of sternal wound reconstruction in the BIMA group.³² In view of our understanding of the timing of vein graft failure it would have been surprising to see any benefit from BIMA grafting at this stage. Further supportive evidence for the beneficial effect of BIMA has been shown from a single centre propensity matched study of 928 BIMA versus 928 LIMA and saphenous vein grafts reporting to 17 years with a survival benefit of 10% at 10 years and 18% at 15 years.³³

There has been great interest in the use of the radial artery as a conduit for coronary artery bypass surgery, with enthusiasts recommending its use, either alongside both internal mammary arteries for a total arterial grafting approach or in addition to a single mammary artery, to improve long-term outcomes. However, a randomised study of 733 patients comparing radial artery grafts to saphenous veins has recently shown similar graft patency at 1 year (both 89%).³⁴ Of concern, the radial artery was associated with a higher incidence of vasospasm in this study and the saphenous vein had better outcomes in diabetic patients. Further concern has been raised from a study using CT scanning to assess graft patency.³⁵ However, there remain a numbers of reports claiming good late patency rates.³⁶⁻³⁸

Most of the studies looking at comparative outcomes of different surgical strategies have relied on late outcomes, with mortality being most important, and these data are obviously difficult to collect and they only provide useful information many years 'after the event'. To help provide useful and more timely differential data, some workers have been looking at techniques to assess preoperative risk other than clinical outcomes such as per-operative injury to the left ventricular myocardium. This is hard to quantify and was the subject of a recent study from Oxford in which 40 patients underwent cardiac MR before and after CABG with serial assessment of troponin I (TnI).³⁹ TnI correlated closely with the mass of new cardiac MR necrosis ($r=0.83$, $p<0.001$), with sensitivity and specificity values of 75% and 87%, making it a robust means of diagnosing this type of MI.

Alongside analyses of ways to optimise operative surgical strategy, there is also an increasing focus on non-mortality postoperative outcomes and pathways. For example, a study published in this journal has examine the implications of postoperative anaemia in a retrospective analysis of 2,553 CABG patients included in the IMAGINE trial.⁴⁰ They showed that postoperative anaemia sustained for >50 days is associated with an increased incidence of cardiovascular events during the first 3 months. The researchers also found that ACE inhibition slowed recovery from postoperative anaemia and increased the incidence of cardiovascular events after CABG, although the mechanism and therapeutic implication of this observation is not clear. It is also become increasingly accepted that formal cardiac rehabilitation is beneficial to enhance recovery after CABG surgery, with an emphasis being placed on exercise programmes. While the best means of delivering these programmes is unclear, a Canadian study favoured a home-based strategy based on a 6-year follow-up of patients randomised to hospital versus telephone-monitored home-based exercise training.⁴¹

nakon CABG, iako mehanizam i terapijske posljedice ovog saznanja nije razumljiva. Također, sve je više prihvaćeno da je formalna kardiološka rehabilitacija korisna za ubrzanje oporavka nakon CABG revaskularizacije, s naglaskom na programe tjelovježbe. Dok su i dalje nepoznati najbolji načini prakticiranja tih programa, kanadska studija bazirana na 6-godišnjem praćenju bolesnika utvrdila je da u randomiziranim skupinama prednost ima kućna tjelovježba monitorirana telefonom u odnosu na bolničku rehabilitaciju.⁴¹

Aortokoronarno premoštenje kod zatajivanja srca?

Studija STICH je utvrdila da ne postoji razlika u preživljavanju između bolesnika sa zatajivanjem srca i lošom funkcijom lijeve klijetke, ako su randomizirani samo na farmakološko liječenje ili na farmakološko liječenje uz CABG. U podskupini ove studije koja je procjenjivala vijabilnost miokarda, prisutnost vijabilnog miokarda je bila povezana s boljim ukupnim preživljavanjem, ali to se nije pokazalo značajnim nakon prilagodbe za ostale osnovne varijable.^{42,43} Promatrajući prave vrijednosti rezultata, radi se o temeljnim spoznajama važnim za kirurgiju aortokoronarnog premoštenja i u sukobu su s predrasudama mnogih liječnika i kirurga. Neka zapažanja se pitaju o iskoristivosti rezultata zbog teškoća s uključivanjem ispitanika koje su dovele do promjene ustroja istraživanja, pored prijelazne stope od 17% za CABG te manje prednosti operativnog zahvata i ukazivanja da se CABG treba razmotriti ako je opseg KBS miokarda težak, a postoji vijabilnost miokarda.⁴⁴ Nedavna studija koje je uspoređivala bolesnika s CABG nasuprot farmakološkoj terapiji (ustrojena poput ključnih kriterija u STICH studiji) pokazala je za 10-godišnje razdoblje jasno produljenje života bolesnika nakon CABG.⁴⁵

Kirurgija aortnog zaliska

Praksa operiranja aortnog zaliska se mijenja. Tijekom 2009. godine u SAD je objavljeno izvješće o analizi 108.687 izoliranih zamjena aortnog zaliska (AVR) u razdoblju od 1997. do 2006. godine.⁴⁶ Uz povećanu primjenom biološkog zaliska, pobol i smrtnost su se smanjili, unatoč postupnom porastu starosti i ukupnog rizika bolesnika. Slični trendovi su se javili u britanskom izvješću kod 41.227 bolesnika u razdoblju od 2004. do 2009. god. s ukupnom bolničkim letalitetom od 4,1%. Godišnji broj se povećava za 20% uz značajno povećanje srednje životne dobi pacijenta s aortnom stenozom, osamnaestogodišnjaka, udjelom visokorizičnih bolesnika i onih kojima se ugrađuju biološki zalisci (koji su gotovo uvijek pod utjecajem stavova kirurga vezanih uz veću dugovječnost modernih bioloških zalistaka uz obećanje o postavljanju zaliska transkateterskim načinom kod idućeg problema sa zaliskom).⁴⁷ Tijekom tog razdoblja bolnička smrtnost je smanjena s 4,4% na 3,7%.⁴⁸ Dok transkateterska implantacija aortne valvule (TAVI) (vidi ispod) utječe na kirurgiju aortne valvule smanjenjem broja tradicionalnih operacija, objavljeno je da se pokretanjem TAVI može povećati ukupan broj operacija aortnog zaliska, uključujući i one kod tradicionalne kirurgije.⁴⁹

Postoje neslaganja o optimalnom vremenu operacije u asimptomatskih bolesnika s aortnom stenozom (vidi paralele s rekonstrukcijom mitralne valvule ispod). Neki obavljani radovi ukazuju na prednosti ranijeg zahvata, a neki su istraživači objavili podatke koji ukazuju na prednosti i nedostatke redovitog praćenja za odabir optimalnog vremena zahvata.⁵⁰⁻⁵³

Transkateterska implantacija zaliska

Posljednjih godina velika promjena u liječenju bolesnika s aortnom stenozom je pojava transkateterske implantacije

Coronary artery surgery for heart failure?

The STICH trial has showed that there is no difference in survival between patients with heart failure and poor left ventricular function, randomised to either medical therapy or medical therapy plus CABG. In a subset of this study in which myocardial viability was assessed, the presence of viable myocardium was associated with better survival overall, but this was not significant after adjusting for other baseline variables.^{42,43} Taken at face value these are profound findings for the practice of coronary artery surgery and are at odds with many physicians and surgeons preconceptions, but some observers have questioned whether the findings of the trial are valid because of difficulties in trial recruitment leading to changes in trial design after instigation alongside a crossover rate of 17% to CABG, therefore underestimating the benefits of surgery and suggesting that CABG should still be considered if CAD is severe and viable myocardium is seen.⁴⁴ For example, a recent propensity matched study of CABG versus medical therapy in these patients (designed to mimic the STICH trial inclusion) showed a clear survival advantage of CABG at 10 years.⁴⁵

Aortic valve surgery

The practice of aortic valve surgery is changing. In the USA, an analysis of 108,687 isolated aortic valve replacement (AVR) patients from 1997 to 2006 was reported in 2009.⁴⁶ Morbidity and mortality have fallen despite gradual increases in patient age and overall risk profile, alongside an increase in biological valve use. Similar trends have been seen in the UK with a report of 41,227 patients between 2004 and 2009 with an overall inhospital mortality of 4.1%. The annual number increased by 20%, with significant increases in the mean age of patients with aortic stenosis, octogenarians, the proportion of high-risk patients and again those receiving biological valves (which is almost certainly influenced by surgeons' views of better longevity of modern biological valves and the promise of a transcatheter valve solution for subsequent valve failure).⁴⁷ Over this time, inhospital mortality decreased from 4.4% to 3.7%.⁴⁸ While transcatheter valve insertion (TAVI) (see below) is having an impact on valve surgery, in contrast to just eroding the numbers of conventional valve operations, it has been reported that starting a TAVI service may increase overall aortic valve interventions, including those for conventional surgery.⁴⁹

There remains some controversy about the timing of surgery in asymptomatic aortic stenosis (see parallels with mitral valve repair below). Some work is being produced suggesting benefits from earlier intervention but other observers have published data suggesting benefits and safety of the watchful waiting approach.⁵⁰⁻⁵³

Transcatheter valve insertion

The major change in the treatment of patients with aortic stenosis in recent years has been the advent of TAVI, which has now been shown to be a good option for the treatment of some patients with aortic stenosis. The Partner study Cohort A trial of 358 patients who were not considered suitable for conventional AVR showed that TAVI decreased the rate of mortality at 1 year (from 51% to 31%) and reduced cardiac symptoms compared with conventional treatment.⁵⁴ The 2-year results have also been reported showing persistent survival advantage, but a high rate of stroke in the TAVI

aortnog zaliska (TAVI), koji se pokazao kao dobar odabir za liječenje nekih bolesnika s aortnom stenozom. Studija *Partner Cohort A* uključila je 358 bolesnika koji nisu bili pogodni za tradicionalnu operaciju AVR, pokazala je da liječenje TAVI smanjuje smrtnost tijekom prve godine (sa 51% na 31%) te srčane simptome u usporedbi s tradicionalnim liječenjem.⁵⁴ Dvogodišnji rezultati su također prikazali postojanost u preživljavanju bolesnika, ali i visoku učestalost moždanog udara unutar TAVI skupine zbog više ishemijskih moždanih udara u prvih 30 dana nakon zahvata te više hemoragijskih događaja nakon toga. Stopa rehospitalizacije u TAVI skupini je iznosila 35%, a u tradicionalnoj skupini 72%. Studije kvalitete života kod pacijenata (primjenom upitnika Kansas City kardiomiopatija i SF-12) ukazale su značajne prednosti unutar TAVI skupine više od jedne godine.⁵⁵ Ekonomska analiza tih podataka ukazala je da je trošak po godini dobivenog života bio zadovoljavajući, unutar prihvatljivih granica.⁵⁶

Također se pokazalo da se TAVI može usporediti s tradicionalnom kirurgijom aortnog zaliska. U studiji *Partner Cohort B* randomizirano je 699 visokorizičnih bolesnika s teškom aortnom stenozom na TAVI ili tradicionalni zahvat.⁵⁷ Nije bilo značajne razlike u smrtnosti unutar 30 dana (3,4% kod TAVI i 6,5% kod tradicionalnog zahvata) ili jedne godine (24,2% TAVI, a 26,8% tradicionalna kirurgija). Dvogodišnji podaci također su pokazali da nema razlike u smrtnosti.⁵⁸ Uočene je različita učestalost komplikacija između skupina, s velikim vaskularnim komplikacijama koje su bile češće kod TAVI te krvarenjem i novonastalom fibrilacijom atrijske kod tradicionalne kirurgije. Mnoštvo velikih studija iz registara također je potvrdilo prihvatljive proceduralne i dugoročne ishode.⁵⁹⁻⁶³

Postupak TAVI sada se obavlja u sve većem broju kroz femoralnu arteriju, transapikalno izravno kroz lijevu klijetku i transaortnim pristupom.⁶⁴⁻⁶⁶ Kao odgovor na potencijalne koristi od manje invazivnih pristupa, postoji također pojačano zanimanje u obavljanju "tradicionalnih" zahvata kroz različite manje rezove uključujući minimalnu sternotomiju, parasternotomiju, uzdužnu sternotomiju te desnu prednju torakotomiju. Različite studije, uključujući iskustva jednog centra te meta-analize, pokazale su da je to moguće sigurno primijeniti u ekspertnim centrima.^{67,68} Osim manje invazivnih metoda, da bi se smanjilo vrijeme postavljanja i omogućila lakša implantacija zaliska kroz male rezove, razvijene su i testirane različite nove aortne valvule koje se implantiraju tehnikama koje ne zahtijevaju suture.^{69,70}

Zaključak vezan uz kirurgiju aortnog zaliska i TAVI je da su sada postignuti zajednički stavovi o primjeni TAVI i da se bolje razumije kako postići optimalne ishode od tradicionalne AVR. Studije iz kliničke prakse su utvrdile da su ishodi kirurških zahvata bolji kod visokorizičnih bolesnika u rukama kirurga s velikim brojem operacija.^{71,72}

Kirurgija mitralnog zaliska

Glavni napredak u razumijevanju kirurgije mitralnog zaliska posljednjih godina vezan je uz rekonstrukciju mitralne valvule. Sada je općeprihvaćeno da je kod većine bolesnika s degenerativnom bolesti mitralne valvule rekonstrukcija zaliska bolja opcija od zamjene, a da bolnička i kasnija smrtnost ovisi o težini simptoma i disfunkciji lijevog ventrikula prije operacije. Britanski rezultati ukazuju da se još uvijek mnogi bolesnici kasno upućuju na liječenje, sa 47% bolesnika uz simptome NYHA III. i IV. funkcionalnog razreda, a u vrijeme zahvata 31% bolesnika ima ejekcijsku frakciju lijeve klijetke <50%.¹

group, due to more ischaemic strokes in the first 30 days after the procedure and more haemorrhagic events thereafter. The rate of rehospitalisation was 35% in the TAVI group and 72% in the conventional group. Quality of life studies on these patients using the Kansas City Cardiomyopathy Questionnaire and the SF-12 showed significant benefits in the TAVI group going out to 1 year.⁵⁵ An economic analysis of these data demonstrated an incremental cost per life-year gained that was well within the acceptable range.⁵⁶

TAVI has also been shown to be comparable with conventional aortic valve surgery. In the *Partner study Cohort B*, 699 patients with severe aortic stenosis who were deemed to be high risk were randomised to TAVI or conventional surgery.⁵⁷ There was no significant difference in mortality rates at 30 days (3.4% TAVI and 6.5% conventional surgery) or 1 year (24.2% TAVI, 26.8% conventional surgery). Two-year data have also been reported, again showing no difference in mortality rates.⁵⁸ Procedural complication rates were different between the groups, with major vascular complications being more common in the TAVI patients and bleeding and new onset atrial fibrillation (AF) more common in conventional surgery. A number of large registry studies have also confirmed acceptable procedural and longer-term outcomes.⁵⁹⁻⁶³

Transcatheter aortic valves are now being inserted in increasing numbers through the femoral artery, trans-apically directly via the left ventricle and through the aortic approach.⁶⁴⁻⁶⁶ In response to potential benefits from less invasive approaches, there has also been increasing interest in conducting 'conventional' surgery through a variety of smaller incisions including mini-sternotomy, para-sternotomy, transverse sternotomy and right anterior thoracotomy. Various studies including single centre experiences and meta-analyses have shown that it can be applied safely in expert centres.^{67,68} Alongside less invasive approaches, to minimise insertion times and allow easier valve implantation through small incisions, various novel aortic valves are being developed and tested which have 'sutureless' implantation techniques.^{69,70}

A final word on aortic valve surgery and TAVI is that there are now consensus statements produced about the practice of TAVI and to understand better how to achieve optimal outcomes from conventional AVR, health service research studies have shown that outcomes of surgery are better for higher risk patients under high volume surgeons, which lay down a challenge for configuration of surgical services for these patients.^{71,72}

Mitral valve surgery

The major advances in understanding of mitral valve surgery in recent years are related to mitral valve repair. It is now well accepted that repair is a better option than replacement for most patients with degenerative mitral valve disease, and that inhospital and later mortality outcomes are dependent on the degree of symptoms and left ventricular dysfunction at the time of surgery. Evidence from the UK suggests that many patients are still being referred late in the disease process with 47% of patients having NYHA class 3 or 4 symptoms and 31% of people displaying left ventricular (LV) ejection fractions of <50% at the time of surgery.¹

Surgical treatment for mitral valve disease is changing over time, and a report on 58,370 patients with isolated mitral regurgitation from the STS database in the 8 years to Decem-

Kirurško liječenje bolesti mitralne valvule se mijenja tijekom vremena, a studija iz STS baze podataka o 58.370 bolesnika s izoliranom mitralnom regurgitacijom tijekom 8 godina do prosinca 2007. godine pokazuje napredak u prihvaćanju mitralne rekonstrukcije umjesto njene zamjene s 51% na 69%. Vremenom je zabilježeno smanjenje uporabe mehaničkih u odnosu na biološke zaliske s 68% na 37% (slični su i britanski podaci).^{1,73} Ovo znači da se jedan od tri bolesnika s teškom mitralnom regurgitacijom podvrgava zamjeni zaliska, a to sa stajališta zdravstva ostaje problem.⁷⁴

Glavna nesuglasica vezana uz bolesnike s teškom mitralnom regurgitacijom je optimalno vrijeme zahvata. Ne postoje randomizirani podaci istraživanja koji bi poduprli bilo ranu operaciju ili "pažljivu procjenu rizika", pa se koriste dokazi dobiveni iz opservacijskih studija. Tijekom 2005. godine *Enriquez-Sarano i sur* s Mayo klinike su objavili opservacijsku studiju kod 456 bolesnika sa simptomatskom organskom mitralnom regurgitacijom koja pokazuje da su pacijenti s efektivnom površinom regurgitacijskog ušća $>40 \text{ mm}^2$ imali preživljavanje tijekom 5 godina manje od očekivanog.⁷⁵ Na temelju toga, kod bolesnika s vrlo teškom mitralnom regurgitacijom oni preporučuju rekonstrukciju mitralne valvule isključivo na temelju simptoma, bez obzira na veličinu ili funkciju lijevog zaliska. Slični rezultati objavljeni su i iz Koreje gdje je 447 uzastopnih asimptomatskih bolesnika podvrgnuto ranom zahvatu ili tradicionalnom obliku liječenja, gdje je rani zahvat povezan s dobrim ishodima dugoročnih događaja smanjenjem kardijalne smrtnosti i hospitalizacije zbog kongestivnog zatajavanja srca.⁷⁶ Sljedeća opservacijska studija koja je tijekom 8,5 godina pratila 192 bolesnika podijeljenih u skupinu s ranim zahvatom i konzervativnu skupinu također je utvrdila bolje ishode u konzervativnoj skupini.⁷⁷

Rosenhek i sur izvijestili su o ishodima istraživanja kod 132 bolesnika s obavljenim intervencijama samo u slučaju pojave simptoma, oštećenja ili značajne dilatacije lijeve klijetke prema prihvaćenim smjernicama.^{78,79} Kasni ishodi su bili izvrsni, a samo je kod trećine bolesnika bio potreban zahvat tijekom razdoblja praćenja od 5 godina, ali je važno da ukoliko se slijedi ova strategija liječenja, pridržavanje mora biti potpuno i sveobuhvatno.

Smjernice Američkog kardiološkog koledža/Američke udruge za srce iz 2006. savjetuju da bi se rani zahvat trebao razmotriti kod asimptomatskih bolesnika s niskim rizikom postupka u "iskusnim centrima" sve dok je vjerojatnost uspješne rekonstrukcije $>90\%$.⁸⁰ Britanska studija pokušala je navesti kriterije povezane s "iskusnim centrima".⁸¹ Međutim, ako pacijent dolazi iz kirurškog epidemiološkog pristupa nužno je razmotriti ukupnu strategiju ranog zahvata.⁷⁴ U studiji s podacima iz STS baze o 13.614 bolesnika s mitralnom regurgitacijom podvrgnutih zahvatu s godišnjim varijacijama broja zahvata, visokovolumni centri imali su veću učestalost rekonstrukcije valvule i manji rizik standardizirane smrtnosti.⁸² U još jednoj studiji iz STS baze u kojoj se analizira 28.507 bolesnika podvrgnutih izoliranoj operaciji mitralne valvule s ili bez operacije trikuspidalne valvule ili popratnog kirurškog liječenja atrijske fibrilacije od strane 1.088 kirurga, prosječna učestalost rekonstrukcija koje su izveli kirurzi je iznosila samo 41%. Medijan godišnjeg broja zahvata je bio 5 (1-166), a povećanje broja zahvata neovisno o tome bilo je povezano s većom vjerojatnosti rekonstrukcije.⁸³ Britanska konsenzus studija smatra da bi se za postizanje optimalnih ishoda operacije u ustanovi godišnje trebalo obavljati više od 50 rekonstrukcija mitralne valvule, a pojedini kirurzi bi ih trebali obaviti više od 25. Čini se da

ber 2007 showed progressive adoption of mitral repair rather than replacement from 51% to 69%. There was also a decrease in the use of mechanical rather than biological valves over that time from 68% to 37% (and there are similar data from the UK).^{1,73} This, of course, indicates that one in three patients with severe MR undergo a valve replacement, and this remains a concern from the perspective of health service delivery.⁷⁴

The major controversy around patients with severe MR is around the timing of surgery. There are no randomised trial data to support early surgery or 'watchful waiting' and so the evidence is derived from observation studies. In 2005, *Enriquez-Sarano and colleagues* from the Mayo Clinic reported an observational study on 456 patients with symptomatic organic mitral regurgitation, showing that patients with an effective regurgitant orifice area of $>40 \text{ mm}^2$ had a survival at 5 years that was lower than expected.⁷⁵ On this basis, they recommended mitral valve repair for patients with genuinely severe mitral regurgitation, purely on the basis of symptoms, irrespective of left ventricular size or function. Similar findings have been reported from Korea on 447 consecutive asymptomatic patients undergoing early surgery or conventional treatment strategy with early surgery associated with improved long-term event rates by decreasing cardiac mortality and congestive heart failure hospitalisation.⁷⁶ A further observational study of 192 patients followed up for 8.5 years, divided into an early surgery and a conservative group, also showed better outcomes in the conservative group.⁷⁷

Conversely, *Rosenhek et al* have reported outcomes on 132 patients and only intervened at the time of onset of symptoms, left ventricular impairment or significant LV dilatation according to the accepted guidelines of the time of onset of symptoms, left ventricular impairment or significant LV dilatation.^{78,79} Overall, late outcomes were excellent, and only a third of patients required surgery during the follow-up period of 5 years, but it is obviously important that if this strategy is followed, follow-up must be robust and comprehensive.

Guidance from the American College of Cardiology/American Heart Association from 2006 suggests that early surgery should be considered for asymptomatic patients at low procedural risk in 'experienced centres' as long as the likelihood of successful repair is $>90\%$.⁸⁰ An attempt has been made from a UK consensus study to describe the criteria associated with an experienced centre.⁸¹ However, if one comes from a surgical epidemiology approach there must be some concern about an overall early surgery strategy for these patients.⁷⁴ In a report of 13,614 patients with mitral regurgitation undergoing surgery from the STS database there was marked variation in overall volumes per year, and higher volume centres showed higher rates of valve repair and lower risk adjusted mortality.⁸² Again from the STS database in an analysis of 28,507 patients undergoing isolated mitral valve surgery with or without tricuspid valve or concomitant AF surgery under 1,088 surgeons, the mean rate of repair by surgeon was only 41%. The median annual number of operation was 5 (1-166) and increasing surgeon volume was independently associated with increased probability of repair.⁸³ The consensus-based opinion study from the UK has suggested that hospitals should be undertaking more than 50 mitral repair operations each year to get optimal outcomes, and individual surgeons should be doing more than 25. It seems that many hospitals and surgeons fall short of this. Offering an early surgical strategy in the absence of

mnoge bolnice i kirurzi to ne mogu postići. Nuditi bolesnicima rani kirurški zahvat uz izostanak jamstva o visokoj stopi oporavka i trajnosti rješenja postupaka rekonstrukcije, ne može biti u njihovom interesu.

Uočeni su neki napredci u tehnikama rekonstrukcije mitralne valvule s pomacima u smjeru češćeg korištenja umjetnih korda i očuvanja tkiva listića, umjesto resekcije i povećanja uporabe manje invazivnih tehnika.⁸⁴⁻⁸⁹ Iako imamo sve više studija koje savjetuju sigurnost minimalno invazivnih pristupa, postoje značajni manji dokazi vezani uz te tehnike i njihovu sigurnost.

Također, tu je i razvoj u smjeru kateterskog načina liječenja mitralne regurgitacije, a EVEREST 2 studija donosi rezultate 78 visokorizičnih bolesnika od tradicionalnog zahvata podvrgnutih bridnom ('edge to edge') liječenju uz pomoć 'MitralClip' sustava, pokazujući stopu smrtnosti postupka od 7,7% uz smanjenje mitralne regurgitacije u većine bolesnika i poboljšanje kliničkih simptoma kod tri četvrtine bolesnika.⁹⁰

Modeliranje rizika

Procjena operativnih rizika u kardijalnoj kirurgiji je važna pri donošenju odluka (npr. tradicionalni zahvat ili TAVI kod bolesnika s aortalnom stenozom), za informirani pristanak bolesnika te za upravljanje i javno izvještavanje o bolničkim i stopama smrtnosti pojedinih kardiokirurga. Nakon analize podataka iz STS baze 2009. godine su objavljeni rezultati STS ljestvice koji imaju modele za revaskularizaciju miokarda, kirurgiju zalistaka te kombinaciju tradicionalnog koronarnog zahvata i kirurgije valvule. Ti modeli predstavljaju standardni skup ishoda kod svih postupaka uključujući smrtnost, moždani udar, reoperacijski zahvat, zatajivanje bubrega, duboku infekciju sternalne rane, prolongiranu ventilaciju, sve glavne pobole, produženi boravak u bolnici i kratak boravak u bolnici.⁹¹⁻⁹⁴

U posljednje vrijeme prihvaćeno je da EuroSCORE nije više pogodan za suvremenu kliničku praksu te je objavljen EuroSCORE 2.^{95,96} Za razliku od modela STS koji su za specifični postupak, EuroSCORE 2 je generički model koji obuhvaća sve kardiokirurške intervencije, što donosi prednosti i mane. Dobiven je iz bolesničke populacije od 22.381 uzastopna bolesnika podvrgnuta velikim kardiokirurškim zahvatima u 154 bolnice iz 43 zemlje u razdoblju od 12 tjedana (svibanj 2010. do srpanj 2010.). Varijable koje su potrebne za dobivanje rezultata ažurirane su iz prethodnog modela te uključuju klirens kreatinina, izmjene kategorizacije ejekcijske frakcije lijeve klijetke i uvođenje polja ograničene mobilnosti.^{96,97} "Težina intervencije" je također različito rješavala problem od originalnog EuroSCORE modela. Istraživači koji razvijaju model izvještavaju o dobroj diskriminaciji i kalibraciji i po svemu sudeći ovaj će model naširoko biti usvojen, ali će to zahtijevati robusno vanjsko vrednovanje. Predstoji rasprava oko načina na koji je izveden i oko uporabe ove vrste modela.⁹⁸

Received: 17th Oct 2012

*Address for correspondence: UHSM, Southmoor Road, Manchester M23 9LT, United Kingdom.

E-mail: ben.bridgewater@uhsm.nhs.uk

Literature

1. Bridgewater B, Kinsman R, Walton P, et al. Demonstrating Quality; The Sixth National Annual Cardiac Database Report. Henley-on Thames: Dendrite Clinical Systems Ltd, 2009.
2. ElBardissi AW, Aranki SF, Sheng S, et al. Trends in isolated coronary artery bypass grafting: an analysis of the Society of Thoracic Surgeons adult cardiac surgery database. *J Thorac Cardiovasc Surg.* 2012;143:273-81.
3. Bridgewater B. Cardiac registers: the adult cardiac surgery register. *Heart.* 2010;96:1441-3.

assurance about high repair rates and excellent durability of repair procedures may not be in the patients' best interests.

There have been some developments in the techniques of mitral valve repair with a move towards more use of artificial chordae tendinae and preservation of leaflet tissue rather than resection and increasing use of less invasive techniques.⁸⁴⁻⁸⁹ While there are a growing number of reports suggesting the safety of minimally invasive approaches, there is significant anecdotal reporting of the concern about these techniques and their safety.

There are also developments in catheter-based treatments of mitral regurgitation, and the Endovascular valve edge to edge repair (EVEREST 2) trial has reported the outcomes of 78 patients at high risk from conventional surgery having an 'edge to edge' treatment with the 'MitralClip' showing a procedural mortality of 7.7% with a reduction in MR in most patients with an improvement in clinical symptoms in three-fourths of the patients.⁹⁰

Risk modelling

The assessment of operative risk in cardiac surgery is important to guide decision making (eg, conventional surgery or TAVI for patients with aortic stenosis), support informed consent and for governance and public reporting of hospital and surgeon mortality rates. The STS scores were published in 2009 after analysing data from the STS database, with models published for coronary artery surgery, valve surgery and combined coronary and valve surgery. These model a standard set of outcomes for all procedures including mortality, stroke, reoperation, renal failure, deep sternal wound infection, prolonged ventilation, composite major morbidity, prolonged length of stay and short length of stay.⁹¹⁻⁹⁴

More recently, it has been accepted that the EuroSCORE is no longer suitable for contemporary practice and the EuroSCORE 2 has been published.^{95,96} Unlike the STS models, which are procedure specific, the EuroSCORE 2 is a generic model covering all cardiac surgery, which has some potential strengths and weaknesses. It was derived from a patient population of 22,381 consecutive patients undergoing major cardiac surgery in 154 hospitals in 43 countries over a 12-week period (May 2010 to July 2010). The fields required to derive the score have been updated from the previous model and include creatinine clearance, modifications to the categorisation of LV ejection fraction and introduction of a limited mobility field.^{96,97} The 'weight of intervention' is also dealt with differently from the original EuroSCORE model. The developers report good discrimination and calibration and it is likely this model will be widely adopted, but it will require robust external validation. There remains debate about the derivation and use of this type of model.⁹⁸

Contributors BB wrote the manuscript.

Competing interests None.

Provenance and peer review Commissioned; internally peer reviewed.

4. Serruys PW, Morice MC, Kappetein AP, et al. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. *N Engl J Med.* 2009;360:961-72.
5. Kappetein AP, Feldman TE, Mack MJ, et al. Comparison of coronary bypass surgery with drug-eluting stenting for the treatment of left main and/or three-vessel disease: 3-year follow-up of the SYNTAX trial. *Eur Heart J.* 2011;32:2125-34.
6. Weintraub WS, Grau-Sepulveda MV, Weiss JM, et al. Comparative effectiveness of revascularization strategies. *N Engl J Med.* 2012;366:1467-76.
7. Lee MS, Yang T, Dhoot J, et al. Meta-analysis of clinical studies comparing coronary artery bypass grafting with percutaneous coronary intervention and drug-eluting stents in patients with unprotected left main coronary artery narrowings. *Am J Cardiol.* 2010;105:1070-5.
8. Naik H, White AJ, Chakravarty T, et al. A meta-analysis of 3,773 patients treated with percutaneous coronary intervention or surgery for unprotected left main coronary artery stenosis. *JACC Cardiovasc Interv.* 2009;2:739-47.
9. Morice MC, Serruys PW, Kappetein AP, et al. Outcomes in patients with de novo left main disease treated with either percutaneous coronary intervention using paclitaxel-eluting stents or coronary artery bypass graft treatment in the Synergy Between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery (SYNTAX) trial. *Circulation.* 2010;121:2645-53.
10. Park SJ, Kim YH, Park DW, et al. Randomized trial of stents versus bypass surgery for left main coronary artery disease. *N Engl J Med.* 2011;364:1718-27.
11. Boudriot E, Thiele H, Walther T, et al. Randomized comparison of percutaneous coronary intervention with sirolimus-eluting stents versus coronary artery bypass grafting in unprotected left main stem stenosis. *J Am Coll Cardiol.* 2011;57:538-45.
12. Capodanno D, Tamburino C. Unraveling the EXCEL: promises and challenges of the next trial of left main percutaneous coronary intervention. *Int J Cardiol.* 2012;156:1-3.
13. Capodanno D, Caggegi A, Capranzano P, et al. Validating the EXCEL hypothesis: a propensity score matched 3-year comparison of percutaneous coronary intervention versus coronary artery bypass graft in left main patients with SYNTAX score <1/432. *Catheter Cardiovasc Interv.* 2011;77:936-43.
14. Wijns W, Kolh P, Danchin N, et al. Guidelines on myocardial revascularization. *Eur Heart J.* 2010;31:2501-55.
15. Ribichini F, Taggart D. Implications of new ESC/EACTS guidelines on myocardial revascularisation for patients with multi-vessel coronary artery disease. *Eur J Cardiothorac Surg.* 2011;39:619-22.
16. Taggart DP, Boyle R, de Belder MA, et al. The 2010 ESC/EACTS guidelines on myocardial revascularisation. *Heart.* 2011;97:445-6.
17. Falk V, Taggart DP. NICE guidance for off-pump CABG: turn off the pump. *Heart.* 2011;97:1731-3.
18. Pepper JR. NICE guidance for off-pump CABG: keep the pump primed. *Heart.* 2011;97:1728-30.
19. Shroyer AL, Grover FL, Hattler B, et al. On-pump versus off-pump coronary-artery bypass surgery. *N Engl J Med.* 2009;361:1827-37.
20. Puskas JD, Mack MJ, Smith CR. On-pump versus off-pump CABG. *N Engl J Med.* 2010;362:851; author reply 53-4.
21. Zenati MA, Shroyer AL, Collins JF, et al. Impact of endoscopic versus open saphenous vein harvest technique on late coronary artery bypass grafting patient outcomes in the ROOBY (Randomized On/Off Bypass) Trial. *J Thorac Cardiovasc Surg.* 2011;141:338-44.
22. Moller CH, Perko MJ, Lund JT, et al. Three-year follow-up in a subset of high-risk patients randomly assigned to off-pump versus on-pump coronary artery bypass surgery: the Best Bypass Surgery trial. *Heart.* 2011;97:907-13.
23. Hueb W, Lopes NH, Pereira AC, et al. Five-year follow-up of a randomized comparison between off-pump and on-pump stable multivessel coronary artery bypass grafting. The MASS III Trial. *Circulation.* 2010;122(Suppl 1):S48-52.
24. Lamy A, Devreux PJ, Prabhakaran D, et al. Off-pump or on-pump coronary-artery bypass grafting at 30 days. *N Engl J Med.* 2012;366(16):1489-97.
25. Kuss O, von Salviati B, Borgermann J. Off-pump versus on-pump coronary artery bypass grafting: a systematic review and meta-analysis of propensity score analyses. *J Thorac Cardiovasc Surg.* 2010;140:829-35, 35 e1-13.
26. Puskas JD, Thourani VH, Kilgo P, et al. Off-pump coronary artery bypass disproportionately benefits high-risk patients. *Ann Thorac Surg.* 2009;88:1142-7.
27. Angelini GD, Culliford L, Smith DK, et al. Effects of on-and off-pump coronary artery surgery on graft patency, survival, and health-related quality of life: long-term follow-up of 2 randomized controlled trials. *J Thorac Cardiovasc Surg.* 2009;137:295-303.
28. Anastasiadis K, Argiriadou H, Kosmidis MH, et al. Neurocognitive outcome after coronary artery bypass surgery using minimal versus conventional extracorporeal circulation: a randomised controlled pilot study. *Heart.* 2011;97:1082-8.
29. Lopes RD, Hafley GE, Allen KB, et al. Endoscopic versus open vein-graft harvesting in coronary-artery bypass surgery. *N Engl J Med.* 2009;361:235-44.
30. Grant SW, Grayson AD, Zacharias J, et al. What is the impact of endoscopic vein harvesting on clinical outcomes following coronary artery bypass graft surgery? *Heart.* 2012;98:604.
31. Ouzounian M, Hassan A, Buth KJ, et al. Impact of endoscopic versus open saphenous vein harvest techniques on outcomes after coronary artery bypass grafting. *Ann Thorac Surg.* 2010;89:403-8.
32. Taggart DP, Altman DG, Gray AM, et al. Randomized trial to compare bilateral vs. single internal mammary coronary artery bypass grafting: 1-year results of the Arterial Revascularisation Trial (ART). *Eur Heart J.* 2010;31:2470-81.
33. Grau JB, Ferrari G, Mak AW, et al. Propensity matched analysis of bilateral internal mammary artery versus single left internal mammary artery grafting at 17-year follow-up: validation of a contemporary surgical experience. *Eur J Cardiothorac Surg.* 2012;41:770-5; discussion 76.
34. Goldman S, Sethi GK, Holman W, et al. Radial artery grafts vs saphenous vein grafts in coronary artery bypass surgery: a randomized trial. *JAMA.* 2011;305:167-74.
35. Levisman JM, Budoff MJ, Karlsberg RP. Long-term coronary artery graft patency as evaluated by 64-slice coronary computed tomographic angiography. *Coron Artery Dis.* 2011;22:521-5.
36. Achouh P, Boutekadji R, Toledano D, et al. Long-term (5-to 20-year) patency of the radial artery for coronary bypass grafting. *J Thorac Cardiovasc Surg.* 2010;140:73-9, 79 e1-2.
37. Hayward PA, Buxton BF. The Radial Artery Patency and Clinical Outcomes trial: design, intermediate term results and future direction. *Heart Lung Circ.* 2011;20:187-92.
38. Hayward PA, Gordon IR, Hare DL, et al. Comparable patencies of the radial artery and right internal thoracic artery or saphenous vein beyond 5 years: results from the Radial Artery Patency and Clinical Outcomes trial. *J Thorac Cardiovasc Surg.* 2010;139:60-5; discussion 65-7.
39. Pegg TJ, Maunsell Z, Karamitsos TD, et al. Utility of cardiac biomarkers for the diagnosis of type V myocardial infarction after coronary artery bypass grafting: insights from serial cardiac MRI. *Heart.* 2011;97:810-16.
40. Westenbrink BD, Kleijn L, de Boer RA, et al. Sustained postoperative anaemia is associated with an impaired outcome after coronary artery bypass graft surgery: insights from the IMAGINE trial. *Heart.* 2011;97:1590-6.
41. Smith KM, McKelvie RS, Thorpe KE, et al. Six-year follow-up of a randomised controlled trial examining hospital versus home-based exercise training after coronary artery bypass graft surgery. *Heart.* 2011;97:1169-74.
42. Velazquez EJ, Lee KL, Deja MA, et al. Coronary-artery bypass surgery in patients with left ventricular dysfunction. *N Engl J Med.* 2011;364:1607-16.
43. Bonow RO, Maurer G, Lee KL, et al. Myocardial viability and survival in ischemic left ventricular dysfunction. *N Engl J Med.* 2011;364:1617-25.
44. Mack MJ. Coronary artery disease: how should the STICH trial results affect clinical practice? *Nat Rev Cardiol.* 2011;8:427-8.
45. Velazquez EJ, Williams JB, Yow E, et al. Long-term survival of patients with ischemic cardiomyopathy treated by coronary artery bypass grafting versus medical therapy. *Ann Thorac Surg.* 2012;93:523-30.
46. Brown JM, O'Brien SM, Wu C, et al. Isolated aortic valve replacement in North America comprising 108,687 patients in 10 years: changes in risks, valve types, and outcomes in the Society of Thoracic Surgeons National Database. *J Thorac Cardiovasc Surg.* 2009;137:82-90.
47. Cockburn J, Trivedi U, Hildick-Smith D. Transaortic transcatheter aortic valve implantation within a previous bioprosthetic aortic valve replacement. *Catheter Cardiovasc Interv.* 2011;78:479-84.
48. Dunning J, Gao H, Chambers J, et al. Aortic valve surgery: marked increases in volume and significant decreases in mechanical valve use: an analysis of 41,227 patients over 5 years from the Society for Cardiothoracic Surgery in Great Britain and Ireland National database. *J Thorac Cardiovasc Surg.* 2011;142:776-82 e3.

49. Grant SW, Devbhandari MP, Grayson AD, et al. What is the impact of providing a transcatheter aortic valve implantation service on conventional aortic valve surgical activity: patient risk factors and outcomes in the first 2 years. *Heart*. 2010;96:1633-7.
50. Kang DH, Park SJ, Rim JH, et al. Early surgery versus conventional treatment in asymptomatic very severe aortic stenosis. *Circulation*. 2010;121:1502-9.
51. Brown ML, Pellikka PA, Schaff HV, et al. The benefits of early valve replacement in asymptomatic patients with severe aortic stenosis. *J Thorac Cardiovasc Surg*. 2008;135:308-15.
52. Le Tourneau T, Pellikka PA, Brown ML, et al. Clinical outcome of asymptomatic severe aortic stenosis with medical and surgical management: importance of STS score at diagnosis. *Ann Thorac Surg*. 2010;90:1876-83.
53. Avakian SD, Grinberg M, Ramires JA, et al. Outcome of adults with asymptomatic severe aortic stenosis. *Int J Cardiol*. 2008;123:322-7.
54. Leon MB, Smith CR, Mack M, et al. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. *N Engl J Med*. 2010;363:1597-607.
55. Reynolds MR, Magnuson EA, Lei Y, et al. Health-related quality of life after transcatheter aortic valve replacement in inoperable patients with severe aortic stenosis. *Circulation*. 2011;124:1964-72.
56. Reynolds MR, Magnuson EA, Wang K, et al. Cost-effectiveness of transcatheter aortic valve replacement compared with standard care among inoperable patients with severe aortic stenosis: results from the placement of aortic transcatheter valves (PARTNER) trial (Cohort B). *Circulation*. 2012;125:1102-9.
57. Smith CR, Leon MB, Mack MJ, et al. Transcatheter versus surgical aortic-valve replacement in high-risk patients. *N Engl J Med*. 2011;364:2187-98.
58. Kodali SK, Williams MR, Smith CR, et al. Two-year outcomes after transcatheter or surgical aortic-valve replacement. *N Engl J Med*. 2012;366:1686-95.
59. Moat NE, Ludman P, de Belder MA, et al. Long-term outcomes after transcatheter aortic valve implantation in high-risk patients with severe aortic stenosis: the U.K. TAVI (United Kingdom Transcatheter Aortic Valve Implantation) Registry. *J Am Coll Cardiol*. 2011;58:2130-8.
60. Zahn R, Gerckens U, Grube E, et al. Transcatheter aortic valve implantation: first results from a multi-centre real-world registry. *Eur Heart J*. 2011;32:198-204.
61. Lefevre T, Kappetein AP, Wolner E, et al. One year follow-up of the multi-centre European PARTNER transcatheter heart valve study. *Eur Heart J*. 2011;32:148-57.
62. Gilard M, Eltchaninoff H, Lung B, et al. Registry of transcatheter aortic-valve implantation in high-risk patients. *N Engl J Med*. 2012;366:1705-15.
63. Ussia GP, Barbanti M, Colombo A, et al. Impact of coronary artery disease in elderly patients undergoing transcatheter aortic valve implantation: insight from the Italian CoreValve Registry. *Int J Cardiol*. Published Online First: 27 March 2012 PMID: 22459391.
64. Eltchaninoff H, Durand E, Borz B, et al. Prospective analysis of 30-day safety and performance of transfemoral transcatheter aortic valve implantation with Edwards SAPIEN XT versus SAPIEN prostheses. *Arch Cardiovasc Dis*. 2012;105:132-40.
65. Bapat V, Khawaja MZ, Attia R, et al. Transaortic Transcatheter Aortic valve implantation using Edwards Sapien valve: a novel approach. *Catheter Cardiovasc Interv*. 2012;79:733-40.
66. Litzler PY, Borz B, Smail H, et al. Transapical aortic valve implantation in Rouen: four years' experience with the Edwards transcatheter prosthesis. *Arch Cardiovasc Dis*. 2012;105:141-5.
67. Murtuza B, Pepper JR, Stanbridge RD, et al. Minimal access aortic valve replacement: is it worth it? *Ann Thorac Surg*. 2008;85:1121-31.
68. Brown ML, McKellar SH, Sundt TM, et al. Ministernotomy versus conventional sternotomy for aortic valve replacement: a systematic review and meta-analysis. *J Thorac Cardiovasc Surg* 2009;137:670-9 e5.
69. Zannis K, Folliguet T, Laborde F. New sutureless aortic valve prosthesis: another tool in less invasive aortic valve replacement. *Curr Opin Cardiol*. 2012;27:125-9.
70. Folliguet TA, Laborde F, Zannis K, et al. Sutureless pericardial aortic valve replacement: results of two European centers. *Ann Thorac Surg*. 2012;93:1483-8.
71. Holmes DR Jr, Mack MJ, Kaul S, et al. 2012 ACCF/AATS/SCAI/STS expert consensus document on transcatheter aortic valve replacement. *J Am Coll Cardiol*. 2012;59:1200-54.
72. Dewey TM, Herbert MA, Ryan WH, et al. Influence of surgeon volume on outcomes with aortic valve replacement. *Ann Thorac Surg*. 2012;93:1107-12; discussion 12-3.
73. Gammie JS, Sheng S, Griffith BP, et al. Trends in mitral valve surgery in the United States: results from the Society of thoracic surgeons adult cardiac surgery database. *Ann Thorac Surg*. 2009;87:1431-7; discussion 37-9.
74. Anyanwu AC, Bridgewater B, Adams DH. The lottery of mitral valve repair surgery. *Heart*. 2010;96:1964-7.
75. Enriquez-Sarano M, Avierinos JF, Messika-Zeitoun D, et al. Quantitative determinants of the outcome of asymptomatic mitral regurgitation. *N Engl J Med*. 2005;352:875-83.
76. Kang DH, Kim JH, Rim JH, et al. Comparison of early surgery versus conventional treatment in asymptomatic severe mitral regurgitation. *Circulation*. 2009;119:797-804.
77. Montant P, Chenot F, Robert A, et al. Long-term survival in asymptomatic patients with severe degenerative mitral regurgitation: a propensity score-based comparison between an early surgical strategy and a conservative treatment approach. *J Thorac Cardiovasc Surg*. 2009;138:1339-48.
78. Rosenhek R, Rader F, Klaar U, et al. Outcome of watchful waiting in asymptomatic severe mitral regurgitation. *Circulation*. 2006;113:2238-44.
79. Rosenhek R. Watchful waiting for severe mitral regurgitation. *Semin Thorac Cardiovasc Surg*. 2011;23:203-8.
80. Bonow RO, Carabello BA, Kanu C, et al. ACC/AHA 2006 guidelines for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines (writing committee to revise the 1998 guidelines for the management of patients with valvular heart disease): developed in collaboration with the Society of cardiovascular Anesthesiologists: endorsed by the Society for cardiovascular angiography and interventions and the Society of thoracic surgeons. *Circulation*. 2006;114:e84-231.
81. Bridgewater B, Hooper T, Munsch C, et al. Mitral repair best practice: proposed standards. *Heart*. 2006;92:939-44.
82. Bolling SF, Li S, O'Brien SM, et al. Predictors of mitral valve repair: clinical and surgeon factors. *Ann Thorac Surg*. 2010;90:1904-11; discussion 12.
83. Gammie JS, O'Brien SM, Griffith BP, et al. Influence of hospital procedural volume on care process and mortality for patients undergoing elective surgery for mitral regurgitation. *Circulation*. 2007;115:881-7.
84. Perier P, Hohenberger W, Lakew F, et al. Toward a new paradigm for the reconstruction of posterior leaflet prolapse: midterm results of the "respect rather than resect" approach. *Ann Thorac Surg*. 2008;86:718-25; discussion 18-25.
85. Gammie JS, Bartlett ST, Griffith BP. Small-incision mitral valve repair: safe, durable, and approaching perfection. *Ann Surg*. 2009;250:409-15.
86. Gammie JS, Zhao Y, Peterson ED, et al. J. Maxwell Chamberlain Memorial Paper for adult cardiac surgery. Less-invasive mitral valve operations: trends and outcomes from the Society of thoracic surgeons adult cardiac surgery database. *Ann Thorac Surg*. 2010;90:1401-8, 10 e1; discussion 08-10.
87. Modi P, Hassan A, Chitwood WR Jr. Minimally invasive mitral valve surgery: a systematic review and meta-analysis. *Eur J Cardiothorac Surg*. 2008; 34:943-52.
88. Cheng DC, Martin J, Lal A, et al. Minimally invasive versus conventional open mitral valve surgery: a meta-analysis and systematic review. *Innovations (Phila)*. 2011;6:84-103.
89. Iribarne A, Russo MJ, Easterwood R, et al. Minimally invasive versus sternotomy approach for mitral valve surgery: a propensity analysis. *Ann Thorac Surg*. 2010;90:1471-7; discussion 77-8.
90. Whitlow PL, Feldman T, Pedersen WR, et al. Acute and 12-month results with catheter-based mitral valve leaflet repair: the EVEREST II (Endovascular Valve Edgeto-Edge Repair) High Risk Study. *J Am Coll Cardiol*. 2012;59:130-9.
91. Shahian DM, Edwards FH. The Society of Thoracic Surgeons 2008 cardiac surgery risk models: introduction. *Ann Thorac Surg*. 2009;88(Suppl 1):S1.
92. O'Brien SM, Shahian DM, Filardo G, et al. The Society of Thoracic Surgeons 2008 cardiac surgery risk models: part 2 isolated valve surgery. *Ann Thorac Surg*. 2009;88 (1 Suppl):S23-42.
93. Shahian DM, O'Brien SM, Filardo G, et al. The Society of Thoracic Surgeons 2008 cardiac surgery risk models: part 3 valve plus coronary artery bypass grafting surgery. *Ann Thorac Surg*. 2009;88(1 Suppl):S43-62.
94. Shahian DM, O'Brien SM, Filardo G, et al. The Society of Thoracic Surgeons 2008 cardiac surgery risk models: part 1 coronary artery bypass grafting surgery. *Ann Thorac Surg*. 2009;88(1 Suppl):S2-22.
95. Choong CK, Sergeant P, Nashef SA, et al. The EuroSCORE risk stratification system in the current era: how accurate is it and what should be done if it is inaccurate? *Eur J Cardiothorac Surg*. 2009;35:59-61.
96. Nashef SA, Roques F, Sharples LD, et al. EuroSCORE II. *Eur J Cardiothorac Surg*. 2012;41:734-44; discussion 44-5.
97. Miceli A, Bruno VD, Capoun R, et al. Mild renal dysfunction in patients undergoing cardiac surgery as a new risk factor for EuroSCORE. *Heart*. 2011;97:362-5.
98. Sergeant P, Meuris B, Pettinari M. EuroSCORE II, illum qui est gravitates magni observe. *Eur J Cardiothorac Surg*. 2012;41:729-31.