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Almanah 2013.: akutni koronarni sindromi

Almanac 2013: acute coronary syndromes

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SAŽETAK: Nestabilni plak u koronarnim arterijama je najčešći uzrok akutnog koronarnog sindroma (AKS) koji se može manifestirati kao nestabilna angina, infarkt miokarda bez elevacije ST-segmenta i infarkt miokarda s elevacijom ST-segmenta (STEMI), ali se također može manifestirati i kao iznenadni srčani zastoj zbog ishemijom izazvane tahiaritmije. Smrtnost AKS je značajno smanjena u posljednjih nekoliko godina, posebice od njegovih najtežih manifestacija, STEMI i srčanog zastoja. Ovaj trend će se najvjerojatnije nastaviti zbog terapijskog napretka novijeg datuma koji uključuje i nove antitrombocitne lijekove kao što prasugrel, tikagrelor i kangrelor.

KLJUČNE RIJEČI: akutni koronarni sindrom, infarkt miokarda s elevacijom ST-segmenta, antitrombocitni lijekovi.

SUMMARY: Unstable coronary artery plaque is the most common underlying cause of acute coronary syndromes (ACS) and can manifest as unstable angina, non-ST segment elevation infarction, and ST elevation myocardial infarction (STEMI), but can also manifest as sudden cardiac arrest due to ischaemia induced tachyarrhythmias. ACS mortality has decreased significantly over the last few years, especially from the more extreme manifestations of ACS, STEMI, and cardiac arrest. This trend is likely to continue based on recent therapeutic progress which includes novel antiplatelet agents such as prasugrel, ticagrelor, and cangrelor.

KEYWORDS: acute coronary syndrome, ST elevation myocardial infarction, antiplatelet agents.

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Uvod

U Sjedinjenim Američkim Državama (SAD) se godišnje hospitalizira oko 1,2 milijuna bolesnika zbog akutnog koronarnog sindroma (ACS)[1]. Primjećeno je smanjenje učestalosti infarkta miokarda sa ST-elevacijom (STEMI).[2,3] O razlozima se može samo nagađati: moguća objašnjenja uključuju smanjenje pušenja, promjenu dobne strukture stanovništva (STEMI je češći u srednjoj dobi, dok se ACS bez elevacije ST-segmenta javlja češće u starijih osoba), ali i češću primjenu terapije statinima. U posljednjih nekoliko godina dolazi do značajnog poboljšanja ishoda nakon preboljelog STEMI u vidu smanjenja smrtnosti, kardiogenog šoka i zatajivanja srca[1]. Slični trendovi prisutni su i kod drugih manifestacija ACS, kao što je iznenadni srčani zastoj (SCA).[4,5] Zapanjujuće je da se sada klinički ishodi za ACS bez elevacije ST-segmenta (NSTE-ACS) čine lošijima nego za STEMI. Međutim, takva je predodžba pogrešna, naime kratkoročni (bolnički) ishod je još uvijek bolji za NSTE-ACS nego za STEMI, dok je dugoročna smrtnost viša kod NSTE-ACS što je vjerojatno posljedica utjecaja različite životne dobi i prisutnih rizika pacijenata sa STEMI i NSTE-ACS: NSTE-ACS bolesnici su uglavnom stariji i češće imaju višežilnu bolest koronarnih arterija (CAD).

Introduction

In the USA every year nearly 1.2 million patients are hospitalised for acute coronary syndrome (ACS)[1]. However, the proportion of ACS with ST elevation myocardial infarction (STEMI)[2,3] appears to be declining. We can only speculate upon the reasons: potential explanations include the reduction in smoking, the age structure of the population (STEMI is more common in middle age while non-ST segment elevation (NSTE-ACS) occurs more in the elderly), and broader use of statin therapy. Over the last few years there has been a significant improvement in outcomes after STEMI in regard to mortality, cardiogenic shock, and heart failure.[1] Similar trends have been seen for other manifestations of ACS, such as sudden cardiac arrest (SCA)[4,5]. Astonishingly, the clinical outcomes for NSTE-ACS now appear to be worse than for STEMI. However, such figures are misleading, and short term (in-hospital) outcome is still better for NSTE-ACS than for STEMI, while the longer term mortality rate is higher for NSTE-ACS, but this is probably influenced by the different age and risk structure of the STEMI and NSTE-ACS populations: NSTE-ACS patients are generally older and often have multivessel (MV) coronary artery disease (CAD).

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Infarkt miokarda s elevacijom ST-segmenta

Glavni razlog poboljšanje ishoda za STEMI tijekom posljednjih desetljeća je veća dostupnost službi za primarnu perkutanu koronarnu intervenciju (PCI), koje pokušavaju kontinuirano poboljšati svoje rezultate ("od vrata do postavljanja balona"). Njihove inicijative uključuju telemetrijski prijenos EKG zapisa iz hitne medicinske pomoći (HMP), kao i obuku osoblja službe HMP za interpretaciju EKG. Naravno, cjelokupno vrijeme od "početka simptoma do postavljanja balona" je važnije od vremena "od vrata do postavljanja balona". Također, bolesnici su bolje informirani o simptomima srčanog udara, a mnoge službe HMP prevoze bolesnike sa sumnjom na STEMI izravno u službu s mogućnosti liječenja primarnom perkutanom koronarnom intervencijom (pPCI), a ne u najbližu bolnicu.

Primarna perkutana koronarna intervencija

Ne samo da je učestalost pPCI porasla tijekom godina, nego je i napredak tehnologije i farmakoterapije doveo do poboljšanja postotka uspješnosti zahvata — prije svega, dostupnost stentova i druge generacije stentova obloženih lijekovima, uređaja za aspiraciju tromba te sigurnijih i učinkovitijih periproceduralnih antikoagulantnih/antitrombocitnih lijekova. Aspiracija tromba je u manjim randomiziranim ispitivanjima pokazala poboljšanje ishoda i preporuča u važećim europskim i američkim smjernicama za perkutanu koronarnu intervenciju (PCI). Međutim, učinak postupka se ne bi trebalo precijenivati. Nedavno provedeno veliko randomizirano INFUSE-AMI istraživanje kod 452 bolesnika nije dokazalo da manualna aspiracija tromba u kombinaciji s bivalirudinom (i intrakoronarnim abciksimabom) utječe na veličinu infarkta miokarda.[6,7] Intravenski inhibitori glikoproteina (Gp) IIb/IIIa imaju izravan i snažan inhibicijski učinak na trombicite i zasigurno poboljšavaju razgradnju tromba; naime, oni mogu smanjiti veličinu infarkta.[6] Međutim, njihov učinak na kliničke ishode je iskutabilan. Bivalirudin, izravni inhibitor trombina, koji ima antikoagulacijske i vjerojatno antitrombocitne učinke (suzbijanjem trombina posredovane aktivacije trombocitima[8]) može se koristiti kao zamjena za heparin i inhibitore Gp IIb/IIIa te je pokazao smanjenje stope krvarenja i smrtnosti u istraživanju HORIZON-AMI[6]. Smanjenje učestalosti krvarenja je glavni cilj u pPCI zbog dobro dokumentirane (ali manje dobro razumljive) povezanosti s povećanim mortalitetom (**Tablica 1**).

Usporedba transradijalnog s transfemoralnim pristupom

Transradijalni pristup je opcija koja se koristi sve češće umjesto tradicionalnog transfemoralnog pristupa i kojom se može smanjiti komplikacije krvarenja9. Naime, sve veći broj podataka ukazuje da se ovim pristupom smanjuje krvarenje općenito, a podaci čak upućuju i na smanjenje smrtnost kada se koristi kod pPCI, no to je diskutabilno. Nedavna meta-analiza koja je obuhvatila devet studija te uključila 2.977 bolesnika sa STEMI je pokazala gotovo 50% smanjenje smrtnosti kod transradijalnog pristupa (OR 0.53, 95% CI 0.33-0.84; p=0,008).[10] Iako su autori zaključili da bi se kod bolesnika sa STEMI trebao preferirati transradijalni pristup, u popratnom uvodniku su istaknuta neka ograničenja tih podataka.[11] Neki podaci ukazuju na negativan utjecaj transradijalne PCI. *Baklanov i sur.*[12] su ukazali da je kod transradijalog PCI duži medijan razdoblja "od vrata do postavlja-

ST elevation myocardial infarction

A major reason for the improved outcomes for STEMI over the last decades has been the increasing availability of primary percutaneous coronary intervention (PCI) services, which all try to continuously improve their performance ('door-to-balloon time'). Initiatives include telemetric transmission of ECGs from the ambulance services, and training of ambulance staff in ECG interpretation. More important than door-to-balloon time is of course the overall 'symptom onset to balloon time'. Patients have become much better informed about symptoms of 'heart attacks', and many ambulance services transfer patients with a suspected STEMI directly to a primary PCI service rather than going to the nearest hospital.

Primary percutaneous coronary intervention

Not only has the rate of primary PCI increased over the years, but progress in device technologies and adjunctive pharmacology has also improved the procedural success rate — for example, the availability of stents and second generation drug eluting stents, thrombus aspiration devices, and safer and more effective periprocedural anticoagulation/antiplatelet treatments. Thrombus aspiration has been shown to improve outcomes in smaller randomised trials and is currently recommended by European and American PCI guidelines. However, its effect should probably not be overrated. A recent large scale randomised trial in 452 patients, INFUSE-AMI (Intracoronary Abciximab and Aspiration Thrombectomy in Patients with Large Anterior Myocardial Infarction) did not demonstrate an effect of manual thrombus aspiration on infarct size when used in conjunction with bivalirudin (and intracoronary abciximab).[6,7] Intravenous glycoprotein (Gp) IIb/IIIa inhibitors have an immediate and potent platelet inhibitory effect and certainly improve thrombus resolution[6]; they may reduce infarct size while their effect on clinical outcomes is somewhat more debatable. Bivalirudin, a direct thrombin inhibitor, which has anticoagulant and probably also antiplatelet effects (via suppression of thrombin dependent platelet activation[8]), can be used as an alternative to heparin and Gp IIb/IIIa inhibitors, and has shown reduced bleeding and even reduced mortality in the HORIZON-AMI trial[6] (Heparin plus a glycoprotein IIb/IIIa Inhibitor versus Bivalirudin Monotherapy and Paclitaxel-Eluting Stents versus Bare-Metal Stents in Acute Myocardial Infarction). Bleeding reduction has become a key aim in primary PCI because of the well documented (but less well understood) association with increased mortality (**Table 1**).

Transradial versus transfemoral access

Another rather elegant option used increasingly, which may reduce bleeding, involves the transradial approach instead of the traditional transfemoral access. An increasing wealth of data indicate that this reduces bleeding in general; some data even suggest that it reduces mortality when used for primary PCI, but the latter effect is debatable. A recent meta-analysis of nine studies involving 2977 patients with STEMI demonstrated an impressive nearly 50% reduction in mortality for the transradial approach (OR 0.53, 95% CI 0.33 to 0.84; p=0.008)[10]. While the authors concluded that the transradial approach should be preferred in STEMI patients, an accompanying editorial highlighted some limitations of these data[11]. Some data indicate a negative impact of transradial PCI. *Baklanov et al*[12] showed a longer median door-to-

Table 1. *Bleeding avoidance strategies.*[9]

Strategy	Comments
Radial instead of femoral access Bivalirudin	Reduces access site bleeding risk (and potentially also mortality in high risk groups) Bivalirudin superior to heparin and glycoprotein IIb/IIIa inhibitors, reduces bleeding (and reduces mortality in STEMI patients)
Fluoroscopy guided puncture for femoral access	High (or low) puncture to be avoided. The femoral head has a consistent relationship with the common femoral artery, and localisation using fluoroscopy is a useful landmark. However, randomised studies failed to show a clinical benefit but were underpowered
Ultrasound guided puncture for femoral access	Fewer vascular complications with this approach in randomised trials
Vascular closure devices	Controversial study results. Increasing evidence pointing towards a positive effect of vascular closure devices, especially if used with bivalirudin
Individualised bleeding risk assessment	Individualised risk assessment and adjustment of clinical practice using risk models, for example, NCDR CathPCI bleeding risk model (bivalirudin, radial access, etc)

NCDR - National Cardiovascular Database Registry; PCI - percutaneous coronary interventions; STEMI - ST elevation myocardial infarction

nja balona". *Cafri i sur.*[13] su pak u retrospektivnoj usporedbi pokazali da su je to razdoblje slično, bez obzira na pristupni put. Čak i kod starijih ljudi gdje je ateroskleroza uznapredovala, čini se da radijalni pristup ne odgađa reperfuziju te ne uzrokuje produljenje razdoblja "od vrata do postavljanja balona"[14]. Postojala je također zabrinutost da se transradijalnim pristupom u odnosu na transfemoralni može povećati rizik od neuroloških komplikacija. Međutim, *Ratib i sur.*[15] su u retrospektivnoj analizi baze podataka Britanskog društva za kardiovaskularne intervencije provedenoj od siječnja 2006. do prosinca 2010. godine, dokazali da ne postoji značajna povezanost između primjene radijalnog pristupa i pojave neuroloških komplikacija.

Zaključno, transradijalna PCI je zasigurno obećavajuća tehnika u rukama iskusnog operatora. Međutim, unatoč prednostima, primjena ovog pristupa je vrlo različita u pojedinim državama. U Francuskoj i Japanu radijalni pristup je dominantan.[11] U Velikoj Britaniji je njegova primjena porasla gotovo četverostruko s 17,2% 2006. na 57% u 2011. godini.[16] S druge strane, SAD ima najnižu stopu usvajanja radijalnog pristupa za PCI na svijetu (samo kod jednog od šest PCI).[17] Međutim, i tamo dolazi do povećanja primjene radijalnog pristupa. U prvom tromjesečju 2007. godine 1,2% PCI su izvedena transradijalnim pristupom; učestalost se povećala na 16.1% u trećem kvartalu 2012. Ne postoji sumnja da je sve veća primjena transradijalne PCI dovela do smanjenja komplikacija pristupnog puta.[12,16-18]

Neki podaci ukazuju da se transradijalnim pristupom može smanjiti smrtnost kod bolesnika sa STEMI, međutim, to nije dokazano i za NSTE-ACS. U RIVAL istraživanju koje je trenutno najveće randomizirano ispitivanje na ovu temu, nije bilo razlike u velikim kliničkim ishodima kod bolesnika s NSTE-AKS.[19] U kohorti visokorizičnih bolesnika s NSTE-ACS uključenih u istraživanje EARLY-AKS nije bilo značajnih razlika u krvarenju ili ishemijskim ishodima u ovisnosti pristupu, radijalnom ili femoralnom.[20]

Prema nedavnom konsensusu Europskog kardiološkog društva (ESC) radijalni pristup se može primijeniti kao rutinski postupak kod stabilnih i nestabilnih bolesnika.21 Kod bolesnika sa STEMI, ESC preporuča transradijalnu PCI tek nakon što se operator upozna s ovim pristupom kod stabilnih bolesnika i u dijagnostičkim postupcima.

balloon time with transradial PCI. Another retrospective comparison by *Cafri et al*[13], however, showed similar door-to-balloon time irrespective of the access route. Even in elderly people, where there is more advanced atherosclerosis, the radial access does not seem to delay reperfusion as it does not lead to any increase in the door-to-balloon time[14]. There have also been concerns that transradial access may increase the risk of neurological complications compared to transfemoral access. However, in a retrospective analysis of the British Cardiovascular Intervention Society database conducted between January 2006 and December 2010, *Ratib et al*[15] have shown that there is no significant association between the use of radial access and the occurrence of neurological complications.

Overall, transradial PCI is certainly a promising technique when used by experienced operators. However, despite its benefits, its use is highly variable across countries. In France and Japan it is the predominant access route[11]. In the UK, its use increased nearly fourfold from 17.2% in 2006 to 57% in 2011[16]. The USA has the lowest rate of radial access adoption for PCI worldwide (only one in six PCIs)[17]. Even here, there has been an increase in use of radial access. In the first quarter of 2007, 1.2% of PCIs were by the transradial approach; this increased to 16.1% in the third quarter of 2012. There is little doubt that the increasing use of transradial PCI has led to a reduction in access site complications[12,16-18].

While some data indicate that the transradial route may reduce mortality in STEMI patients, this has not been demonstrated in NSTE-ACS. In the RIVAL (Radial vs Femoral Ac cess for Coronary Intervention) trial, currently the largest randomised trial on this topic, there was no difference in major clinical outcomes in NSTE-ACS patients[19]. In a cohort of high risk NSTE-ACS patients enrolled in the EARLY-ACS trial (Early Glycoprotein IIb/IIIa Inhibition in non-ST-Segment Elevation Acute Coronary Syndrome), there were no significant differences in either bleeding or ischaemic outcomes whether radial or femoral access was used[20].

A recent consensus statement by the European Society of Cardiology (ESC) states that a default radial approach is feasible in routine practice in both stable and unstable patients. The ESC recommends performing transradial PCI in STEMI patients only after the operator has become familiar

Perkutana koronarna intervencija kritične lezije

Predmetom rasprave i dalje ostaje pitanje da li rješavati samo kritičnu leziju ili pristupiti potpunoj revaskularizaciji. Moglo bi se reći na sljedeći način: strategija kompletne revaskularizacije može poboljšati ukupnu perfuziju miokarda u kritičnoj početnoj fazi; ali s druge strane, većina glavnih komplikacija se povećava tijekom akutne PCI, što može utjecati i na ishod liječenja neakutnih, nekritičnih lezija. Randomizirana studija na 214 bolesnika je pokazala da je intervencija samo na krvnoj žili s kritičnom lezijom bila povezana s višom učestalosti neželjenih događaja (50,0%) tijekom prosječnog praćenja od 2,5 godina u odnosu na višežilnu PCI, bez obzira na istovremenu potpunu revaskularizaciju (23,1%) ili potpunu revaskularizaciju u fazama (20,0%).[22] Nedavno izvješće japanskog registra Ibaraki Cardiovascular Assessment Study ukazalo je na znatno veću smrtnost kada je istodobno učinjena PCI nekritične i kritične lezije, nasuprot intervencije na samo kritičnoj leziji.[23] Nasuprot tome, rezultati koji se temelje na američkom registru NCDR-CathPCI su pokazali slične stope morbiditeta i mortaliteta kod jednožilne ili višežilne PCI.[24] Navedeni podaci su konroverzni te se napominje da je većina studija nerandomizirana te ih treba tumačiti s oprezom. Velika meta-analiza koja je obuhvatila 18 randomiziranih kontroliranih ispitivanja i uključila 40.280 bolesnika pokazala je da je PCI u fazama bio povezan s nižom kratkoročnom i dugoročnom smrtnošću u odnosu na intervenciju kritične lezije iili višežilni PCI[25]. Zaključno, važeće smjernice ne preporučuju izvođenje PCI na više žila kod STEMI te preporučaju rješavanje nekritičnih lezija u fazama.[26,27] Međutim, ako su bolesnici sa STEMI u slici kardiogenog šoka ili prežive iznenadni srčani zastoj trebala bi se razmotriti kompletna revaskularizacija u jednom aktu.

Utjecaj vremena

U važećim smjernicama ESC preporučuje se transport bolesnika sa STEMI bez odgode u centar u kojem se može učiniti PCI u roku od 2 sata od početka simptoma.[28] U kliničkoj praksi je vrlo teško postići taj cilj.[29] Na temelju rezultata prosječnog praćenja od 3,4 godine kod bolesnika sa STEMI odgađanje liječenja zbog pPCI povezano je s povećanom smrtnošću.[30] U novijoj studiji ukoliko se skrati vrijeme od početka simptoma do postavljanja balona predviđa se dugoročno smanjenje učestalosti smrtnosti.[31] Odgoda liječenja je češće zabilježena kod žena, bolesnika koji žive u ruralnom području >22 km od bolnice i kod bolesnika pregledanih u hitnim službama bolničkih ustanova u odnosu na izravan transfer vozilom HMP. Istraživači ukazujuda bi se većom općom primjenom HMP smanjila odgoda liječenja i uz to povezana smrtnost.

Optimalno trajanje bolničkog liječenja

Duljina bolničkog liječenja tijekom godina se je dramatično smanjila, što uvelike utječe na izdvajanje za zdravstvenu skrb i na kvalitetu bolesnikova života. Trenutna praksa je vrlo različita među zemljama i centrima te ostaje nejasno da li je rani otpust iz bolnice siguran.[32] Ohrabrujuće je da su unatoč kontinuiranom smanjenju duljine boravka u bolnici ishodi liječenja znatno poboljšani (**Slika 1**).

with this approach in stable patients and in diagnostic procedures.

Culprit lesion PCI

Culprit lesion only treatment versus a 'complete revascularisation' approach remains the subject of some debate. One could argue either way: a complete revascularisation strategy may improve overall myocardial perfusion in the critical initial phase; but on the other hand, we know that major adverse complications are increased during acute PCI, and this also may have an impact on the outcome following treatment of non-acute, non-culprit lesions. A randomised study of 214 patients showed that angioplasty of the culprit vessel only was associated with higher rates of adverse events (50.0%) during a mean follow up of 2.5 years than MV PCI, regardless of simultaneous complete revascularisation (23.1%) or a staged complete revascularisation (20.0%)[22]. A recent report of the Ibaraki Cardiovascular Assessment Study registry of Japan showed significantly higher mortality with PCI of a non-culprit lesion in the same setting as the culprit lesion than with PCI of only the culprit lesion[23]. In contrast, results based of the American College of Cardiology National Cardiovascular Database Registry (NCDR-CathPCI) showed similar morbidity and mortality rates with either single vessel or MV PCI[24]. While these data were conflicting, most studies were non-randomised and need to be interpreted with caution. A large meta-analysis of 18 randomised controlled trials (RCTs), including the above mentioned RCT, involved 40 280 patients and showed that staged PCI was associated with lower short and long term mortality compared to culprit vessel PCI and MV PCI[24]. Therefore, current guidelines discourage the performance of multivessel PCI for STEMI and suggest that non-culprit lesions should be staged[26,27]. However, if STEMI patients present in cardiogenic shock or after an SCA, they should be considered for complete revascularisation in one sitting.

The time effect

The current ESC guidelines recommend that STEMI patients should be immediately transported within 2 h of onset of symptoms to a PCI-capable centre without delay[28]. In clinical practice, it is extremely difficult to achieve this goal of symptom onset-to-balloon time[29]. System delays have been shown to be associated with mortality at a median follow-up of 3.4 years in STEMI patients treated with primary PCI[30]. In a more recent study, shorter symptom onset-to-balloon time predicted lower mortality in the long term[31]. A longer treatment delay was seen in females, patients living in a rural area >22 km from hospital, and when patients were admitted to the emergency department of the hospital instead of direct emergency medical services (EMS) transportation. Researchers suggest that a more generalised use of ambulance/EMS would reduce treatment delays and associated mortality.

Optimal duration of monitoring/hospital stay

The duration of hospital stay has decreased dramatically over the years, which has a major impact on health care expenditure and on patient quality of life. Current practice is widely variable across countries and centres, but it is unclear whether early hospital discharges are safe[32]. It is very reassuring that, despite the continuous reduction in hospital stay, outcomes have significantly improved (**Figure 1**).

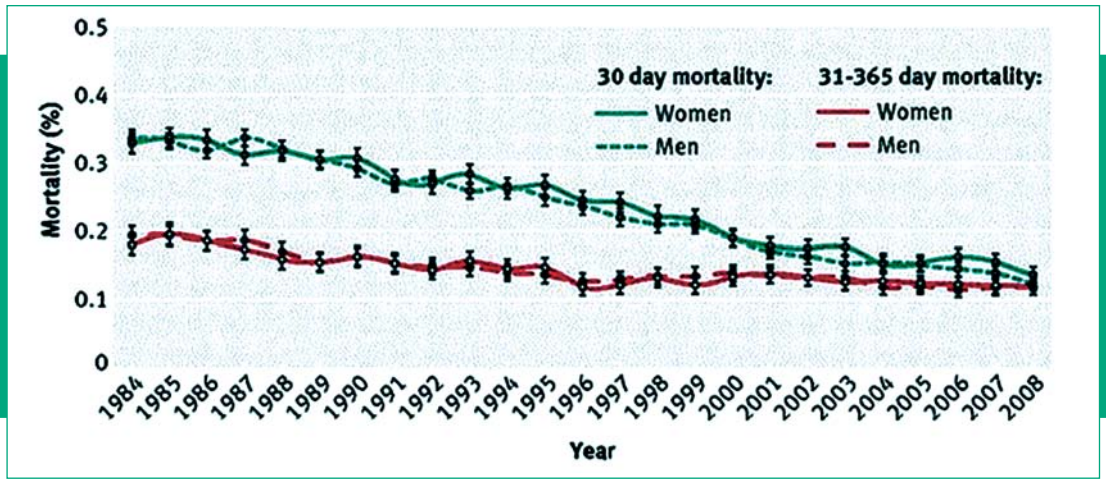

Figure 1. *Change in short and intermediate term mortality after ST elevation myocardial infarction. Standardised 30 day and 31-365 day mortality after first hospitalisation for myocardial infarction among men and women between 1984 and 2008 in Denmark33. Reprinted with permission from BMJ Publishing Group.*

Dvije nove studije su pokazale da je otpust niskorizičnih bolesnika sa STEMI dva dana nakon pPCI sigurno i izvedivo.[34,35] U jednoj od studija više od 40% bolesnika sa STEMI je ispunilo kriterije ranog otpusta.[34] Ranim otpustom iz bolnice se mogu značajno smanjiti troškovi zdravstvene skrbi.

Na temelju literaturnih navoda, predlažemo sljedeće kriterije za definiranje niskorizičnih bolesnika za rani otpust:

1. životna dob <70 godina
2. kratko razdoblje od početka boli do reperfuzije (<4 h)
3. nekomplicirana pPCI s dobrim rezultatom — TIMI (Thrombolysis in Myocardial Infarction) protok) 3 i brzim kompletnim povlačenjem ST-elevacije.
4. EF lijeve klijetke >45% bez simptoma srčanog zatajivanja
5. bez značajnih aritmija tijekom prva 24 sata
6. bolesnik koji ima potporu okoline, koji je suradljiv, koji prihvaća stanje.

AKUTNI KORONARNI SINDROM BEZ ST-ELEVACIJE

Predviđanje rizika

Danas postoji velika potreba za pravilnom stratifikacijom rizika u bolesnika s ACS radi donošenja kliničkih odluka, osobito s obzirom na koronarnu angiografiju. U uporabi su nekoliko modela predviđanja rizika. Jedan od najčešće korištenih modela je GRACE. Nedavno je razvijen model mini-GRACE (MG) koji se razlikuje od izvornog osam faktornog GRACE modela po isključenju iz procjene vrijednosti kreatinina i stupnja prema Killip ljestvici. Prilagođeni mini-GRACE model (AMG) uključuje 'propisivanje diuretika Henleove petlje prilikom prijama" umjesto stupnja prema Killipu i vrijednosti kreatinina. Oba modela procjene rizika su pokazale dobru preciznost u rezultatima nacionalnog istraživanja MINAP, s napomenom da AMG model osigurava nešto bolje rezultate od MG modela.[36]

Laboratorijski markeri mogu dodatno pomoći u stratifikaciji rizika. Maksimalna vrijednost troponina u bolesnika s NSTE-ACS se pokazala kao neovisni prediktor bolničkog morbiditeta i mortaliteta.[37] Ostali prediktivni markeri uključuju interleukin 10, mijeloperoksidazu i faktor rasta posteljice[38].

Two new studies have demonstrated that discharging low risk STEMI patients within 2 days following primary PCI is safe and feasible[34,35]. Over 40% of the STEMI patients in one of the studies met early discharge criteria[34]. An early discharge could lower healthcare costs considerably.

Based on the literature, we propose the following criteria to define low risk patients for early discharge:

1. Age <70 years
2. Short pain to reperfusion interval (<4 h)
3. Uncomplicated primary PCI with good result — TIMI (Thrombolysis in Myocardial Infarction) 3 flow and prompt complete ST elevation resolution)
4. Left ventricular ejection fraction >45% without symptoms of heart failure
5. No significant arrhythmias during the first 24 h
6. Socially supported, collaborative/compliant patient.

NON-ST ELEVATION ACS

Risk prediction

There is a great need for proper risk prediction in ACS patients for clinical decision making, especially with regard to coronary angiography. There are several risk prediction models in use. The Global Registry of Acute Coronary Events (GRACE) is among the most commonly used scores. Recently, a mini-GRACE (MG) risk score has been developed which excludes creatinine and Killip class from the original eight-factor GRACE risk model. The adjusted mini-GRACE (AMG) risk score includes 'prescription of a loop diuretic during admission' in place of Killip class and creatinine concentration. Both risk scores showed good accuracy in the Myocardial Ischaemia National Audit Project (MINAP), with the AMG risk score performing somewhat better than the MG risk score[36].

Laboratory markers may further help with this risk stratification. The maximal troponin value in patients presenting with NSTE-ACS has been shown to be an independent predictor of in-hospital morbidity and mortality[37]. Other predictive markers include interleukin 10, myeloperoxidase, and placental growth factor[38].

Uloga i vrijeme perkutane koronarne intervencije kod akutnog koronarnog sindroma bez ST-elevacije

U bolesnika srednjeg do visokog rizika postoje jaki dokazi koji daju prednost angiografiji nad konzervativnim liječenjem. Međutim, nejasno je kada je optimalno vrijeme za učiniti koronarnu angiografiju. Iako se rani invazivni pristup čini kao prednost, studije koje proučavaju utjecaj vremena na ishod koriste različite vremenske točke za 'rane' i 'odgođene' angiografije. U jako visokorizičnih bolesnika, kao što su to oni s refraktornom anginom, teškim zatajivanjem srca, po život ugrožavajućim ventrikulskim aritmijama ili hemodinamskom nestabilnošću i infarktom miokarda (MI) u pogoršanju, indicira se urgentni invazivni pristup. Za bolesnike koji ne pripadaju u visokorizične, optimalno vrijeme angiografije nije jasno. Ne postoji jasna prednost rane invazivne strategije unutar 24 h u odnosu na značajnije kliničke ishode, unatoč tome sve je veći broj centara koji za bolesnike srednjeg do visokog rizika poduzimaju ranu invazivnu strategiju u roku od 24 sata. Takav pristup je razuman, jer rana intervencija zasigurno dovodi do skraćenja bolničkog liječenja. Čimbenici kao što su dijabetes, renalna funkcija, funkcija lijeve klijetke, učestali simptomi i prethodna revaskularizacija se moraju razmotriti zajedno s procjenom rizika modelima TIMI ili GRACE.

Intravaskularno oslikavanje

Perkutana koronarna intervencija vođena intravaskularim oslikavanjem je koncept koji se razvio dostupnošću uređaja, kao što su intravaskularni ultrazvuk (IVUS) te optička koherentna tomografija (OCT). Intravaskularno oslikavanje se može koristiti prije planirane PCI radi procjene koronarnog plaka (stabilni ili nestabilni plak, promjer i duljina, opterećenje trombom, itd.), ili poslije PCI, radi procjene ekspanzije stenta i apozicije. Prednosti su očite. Nasuprot angiografiji kojom se promatra i omogućuje mjerenje dijametara lumena u nekoliko ortogonalnih projekcija, koronarni IVUS pruža tomografski pregled te bolju rezoluciju nego angiografija.

Prvi puta je koncept procjene lezije prije PCI bio ispitan u multicentričnoj studiji PROSPECT[39]. Ova je studija pokazala da se IVUS može koristiti za definiranje karakteristika vulnerabilnih plakova. Izgled visokorizičnih plakova povezanih s značajnim kardiološkim događajima (MACE) su uključivali fibroaterome s tankom kapom, plakom većim od 70% minimalnim lumenom <4,0 mm. Međutim, podaci o karakteristikama plaka dobiveni oslikavnjem IVUS nisu dostatni za donošenje odluke o potrebi liječenja lezije[40].

Optička koherentna tomografija (OCT) se temelji na primjeni svjetla kraće valne duljine čime se postiže 10 puta bolja rezolucija u usporedbi s oslikavanjem pomoću IVUS koja se temelji na primjeni ultrazvuka.[41] Zbog navedenoga OCT omogućuje bolju definiciju tankih fibroznih kapa i opsega nekrotičnih jezgri te pomaže u otkrivanju drugih mikrostrukturalnih značajki kao što su kristali kolesterola, trombi, naslage kalcija, fibrozni plakovi i plakovi bogati lipidima.[42] OCT također može vizualizirati značajke koje se ne vide primjenom IVUS, kao što su intimalni flapovi i defekti u intimi, prekidi u mediji te apozicija mrežice stenta.

Japanska studija koja je analizirala kritične lezije kod bolesnika s akutnim MI i dokazala je da je učestalost rupture plaka utvrđene OCT veća nego li kod primjene angiografije i IVUS.[43] Također, OCT bio je bio superioran u otkrivanju erozije fibrozne kape i fibroateroma s tankom kapom uz mogućnost procjene debljine fibrozne kape.

Role and timing of PCI in NSTE-ACS

For intermediate to high risk patients, there is strong evidence supporting routine angiography rather than conservative management. However, the optimal time for coronary angiography is not clear. Though an early invasive approach seems favourable, studies testing the timing effect used varying time points for 'early' and 'delayed' angiography. In very high risk patients such as those with refractory angina, severe heart failure, life threatening ventricular arrhythmias or haemodynamic instability or an evolving myocardial infarction (MI), an urgent invasive approach is indicated. For patients not belonging to this high risk category, the optimal timing is not clear. There is no clear benefit with regard to 'hard' clinical end points for an early invasive strategy within 24 h, but an increasing number of centres undertake an early invasive strategy within 24 h for intermediate to high risk patients. Such an approach is probably reasonable, as an earlier approach certainly helps to reduce hospital stay. Factors such as diabetes, renal function, left ventricular function, recurrent symptoms, and previous revascularisation should be considered along with the TIMI or GRACE score.

Intravascular imaging

Intravascular imaging guided PCI is a concept that evolved when devices such as intravascular ultrasound (IVUS) and more recently optical coherence tomography (OCT) became available. There are two different modes of use, either for the pre-PCI assessment in order to better understand the coronary plaque (stable or unstable plaque, diameter and length, thrombus burden, etc), or for post-PCI assessment of stent expansion and apposition. The advantages are obvious; in contrast to angiography as an eyeballing tool, which allows measurement of luminal diameters in a few orthogonal views, coronary IVUS provides a tomographic view. Furthermore, the resolution is much better than for angiography.

The first concept, pre-PCI assessment of lesions has been tested in the multicentre PROSPECT[39] (Providing Regional Observations to Study Predictors of Events in the Coronary Tree) study. This study showed that IVUS can be used to define characteristics of vulnerable plaques. The highest risk phenotypes associated with non-culprit major adverse cardiac events (MACE) included thin-cap fibroatheromas, plaque burden >70%, and minimal lumen area <4.0 mm. However, these data are not sufficient to advocate using IVUS derived plaque characteristics to decide whether a lesion needs to be treated[40].

While IVUS is based on ultrasound, OCT is based on light, which has a much shorter wavelength, and therefore achieves 10-fold better spatial resolution compared to IVUS[41]. This allows better definition of the thin fibrous caps and the circumferential extent of the necrotic cores. It helps detect other microstructural features such as cholesterol crystals, thrombus, calcium deposits, fibrous plaques, and lipid-rich plaques[42]. OCT can visualise features not seen by IVUS such as intimal flaps and defects in the intima, disruptions in the media, and stent strut apposition.

A Japanese study that analysed the culprit lesion in AMI patients found that the incidence of plaque rupture observed by OCT was significantly higher than that observed by both angioscopy and IVUS[43]. OCT was also superior in detecting fibrous cap erosion and thin cap fibroatheroma, and OCT could also estimate the fibrous cap thickness.

Međutim, ova nova tehnika snimanja je ograničena dubinom penetracije na samo nekoliko milimetara.[44] Dakle, njome se ne može snimiti adventicija i procijeniti proširenost plaka. Stoga su *Alfonso i sur.*[45] imali ideju kombinirane primjene OCT i IVUS u bolesnika s trombozom stenta. Budući da je duljina snimke bila kraća s OCT predložili su tehniku preklapanje OCT radi premoštenja tog problema. Značajka OCT je to da za snimanje zahtijeva polje bez krvi.

Metodom OCT, obzirom da je njegova rezolucija bolja u odnosu na IVUS, može se jasno, vidjeti mrežica stenta u jako kalcificiranom području što nije moguće pomoću IVUS. Primjenom OCT poslije intervencije se također dobiva jasnija slika granice neointime i tromba te se može dobiti pouzdana dijagnoza in-stent restenoze i neoateroskleroze. U svakodnevnoj praksi se čini da su OCT i IVUS komplementarne metode sa svojim prednostima i nedostacima. Međutim, treba biti svjestan da su podaci o kliničkim ishodima njihove primjene ograničeni i da primjena navedenih tehnika povećava troškove postupka.

Antitrombocitna terapija

Acetilsalicilatna kiselina (ASK) je još uvijek temelj svake antitrombocitne terapije. Međutim, dualna antitrombocitna terapija ASK i blokatorom P2Y12 receptora je puno učinkovitija, a klopidogrel je u ovom trenutku najčešće korišteno lijek za tu svrhu. Međutim, problem ovog liječenja je duže razdoblje prije početka maksimalne inhibicije trombocita i visoka učestalost onih koji lošije reagiraju na terapiju.[46] Trostruka antitrombocitna terapija primjenom cilostazola testirana je u više navrata, a unatoč nekim pozitivnim rezultatima koristi se rijetko.[47,48] Jedan od razloga za to je vjerojatno razvoj novije generacije blokatora P2Y12 receptora poput prasugrela, tikagrelora i kangrelora koji inhibiraju agregaciju trombocita blokirajući vezivanje ADP na receptore trombocita P2Y12.

Naravno, može se očekivati da snažnija antitrombocitna inhibicija dovodi do povećanog rizika od krvarenja zbog čega mnogi bolesnici uzimaju inhibitore protonske pumpe (PPI). Međutim, podaci ne prate u potpunosti navedeno razmišljanje.

Prasugrel: U TRITON TIMI 38 istraživanju uspoređeni su ASK s prasugrelom naspram ASK s klopidogrelom u 13.608 bolesnika s ACS koji su bli podvrgnuti PCI, a imali su umjeren ili visok rizik. U većini slučajeva ispitivani lijek je dan nakon koronarne angiografije. Nakon 15 mjeseci praćenja veliki neželjeni kardiovaskularni ishodi (MACE; kardiovaskularna smrt, ne-fatalni MI, nefatalni moždani udar) su smanjeni u skupini s prasugrelom (9,9% : 12,1%; HR 0,81, 95% CI 0,73-0,90). Ovakav krajnji rezultat je uglavnom posljedica smanjenja nefatalnih MI. Učestalost velikih krvarenja je porasla s prasugrelom (2,4% : 1,8%; HR 1,32, 95% CI 1,3-1,68). Krvarenje je bilo učestalije u bolesnika s preboljelim moždanim udarom, tranzitornom ishemijskom atakom, dobi ≥75 god. i tjelesne težine ≤60 kg. U istraživanju TRILOGY AKS ispitivala se učinkovitost prasugrela naspram klopidogrela u bolesnika s NSTE-ACS koji nisu bili liječeni PCI. Nije bilo statistički značajnih razlika u učestalosti MACE(13,9% : 16,0%; HR 0.91, 95% CI 0,79-1,05).

Tikagrelor: Za razliku od klopidogrela i prasugrela tikagrelor se reverzibilno veže na P2Y12 trombocitne receptore. Ovaj lijek je ispitivan u PLATO studiji (18.624 bolesnika) u bolesnika s ACS te u onih koji nisu bili liječeni PCI već samo farmakološkom terapijom. Lijek je u terapiju uveden rano, medijan je iznosio 5 sati nakon hospitalizacije. Studija je pokazala smanjeni rizik MACE (definiranih kao kardiovaskularna

However, the depth of imaging penetration is limited to only a few millimetres with this new technique[44]. So, it is unable to image the adventitia and assess the plaque burden. Therefore, *Alfonso et al*[45] had the idea of a combined use of OCT and IVUS in patients with stent thrombosis. Since image length was shorter with OCT, they suggested overlapping OCT runs to circumvent the problem. The challenge of OCT is that it requires a field clear of blood for imaging.

Because OCT has superior resolution to IVUS, it clearly recognises stent struts on heavily calcified areas which are difficult to identify with IVUS. Post-intervention OCT also produces a sharper image of the neointimal-thrombus boundary and provides a reliable diagnosis of in-stent restenosis or neoatherosclerosis. In current practice, OCT and IVUS seem to complement each other with their respective advantages and disadvantages. However, we have to be aware that data on clinical outcomes are limited and that these techniques add to procedural costs.

Antiplatelet therapy

Aspirin is still the basis of every antiplatelet therapy. However, dual antiplatelet therapy of aspirin and a P2Y12 receptor blocker is clearly more effective and clopidogrel is the most commonly used agent for this purpose at the moment. However, the problems with this treatment are the rather long delay until maximal platelet inhibition is reached and the high rate of poor responders[46]. One approach that has been tested repeatedly is triple antiplatelet therapy using cilostazol. Even though results of this approach have indicated some benefit, it is rarely used[47,48]. One reason for this is probably the development of newer generation P2Y12 receptor blockers such as prasugrel, ticagrelor, and cangrelor. They block the binding of ADP to the platelet receptor P2Y12, thereby inhibiting platelet aggregation.

Naturally, we would expect that stronger antiplatelet inhibition comes with an increased bleeding risk. Many patients therefore receive proton pump inhibitors (PPI). However, the data do not completely following this logic.

Prasugrel: The TRITON-TIMI 38 trial was a head-to-head comparison between aspirin and prasugrel versus aspirin plus clopidogrel in 13 608 moderate to high risk ACS patients undergoing PCI. In most cases, the study drug was given after coronary angiography. At 15 months follow-up, MACE (cardiovascular death, non-fatal MI, or non-fatal stroke) was reduced with prasugrel (9.9% vs 12.1%; HR 0.81, 95% CI 0.73 to 0.90) This composite end point was mainly driven by a reduction in non-fatal MI. Major bleeding was somewhat increased with prasugrel (2.4% vs 1.8%; HR 1.32, 95% CI 1.3 to 1.68). Bleeding was mainly increased in those with a history of stroke or transient ischaemic attack, age ≥75 years or a bodyweight ≤60 kg. The TRILOGY ACS trial tested prasugrel versus clopidogrel with NSTE-ACS not undergoing PCI. There was no statistically significant difference in MACE rate (13.9% vs 16.0%; HR 0.91, 95% CI 0.79 to 1.05).

Ticagrelor: In contrast to clopidogrel and prasugrel, ticagrelor binds reversibly to the P2Y12 platelet receptor. This agent was tested in the PLATO trial (18,624 patients) in patients with ACS, and also those who did not undergo PCI but had medical therapy. Treatment was started early, at a median of 5 h after hospital admission. This study showed a reduced risk for MACE (defined as cardiovascular death, MI, or stroke) in the ticagrelor arm (9.8% vs 11.7%, HR 0.84,

smrt, MI, moždani udar) u skupini s tikagrelorom (9,8% : 11,7%, HR 0,84 , 95% CI 0,77-0,92), kao i smanjenje kardiovaskularnog mortaliteta kao pojedinačnog ishoda. Zaključno, nije bilo značajnih razlika u zastupljenosti velikih krvarenja između skupina tikagrelora i klopidogrela (11,6% : 11,2%). Međutim, postoji povećani rizik od većih krvarenja kod nekoronarnih arterijskih premoštenja (4,5% : 3,8%).

Kangrelor: Za razliku od drugih lijekova, kangrelor se daje intravenozno. On je bio ispitivan u usporedbi s placebom i klopidogrelom. Istraživanje CHAMPION-PLATFORM (kontrola placebom) je zaustavljeno ranije zbog razočaravajuće rezultate rane analize. Niti istraživanje CHAMPION-PCI (u usporedbi s klopidogrelom) nije pokazalo značajnu dobrobit. Istraživanje CHAMPION-PHOENIX je najnovija i najveća studija u kojoj se je uspoređivao cangrelor nasuprot dozi zasićenja klopidogrela od 300-600 mg. Ova studija je uključivala pacijente s AKS te stabilnom koronarnom bolesti srca. Njome je utvrđeno smanjenje rizika od ishemijskih događaja tijekom prvih 48 sati (smrt, MI, revaskularizacija zbog ishemije ili tromboza stenta) bez povećanja incidencije značajnih krvarenja.[49] Značenje kangrelora u kliničkoj praksi još uvijek nije jasno, tim više što postoji šira upotreba tikagrelora i prasugrela s kojima on nije bio uspoređivan.

S obzirom na dostupnost nove i snažne antitrombocitne terapije izazov je odlučiti koji lijek koristiti i kada. Trenutno se odluka obično temelji na kliničkim i rizičnim faktorima; u budućnosti će farmakogenetika vjerojatno imati ulogu kod odabira terapije.[50]

Jedna od najčešćih komplikacija snažne antitrombocitne terapije je gastrointestinalno (GI) krvarenje zbog čega se često propisuju PPI. Zanimljivo je da je nedavno istraživanje pokazalo da su krvarenja donjeg dijela GI trakta kod bolesnika na terapiji s PPI češća nego krvarenja gornjeg dijela GI trakta.[51] Utjecaj PPI na učinak klopidogrela je kontroverzan već neko vrijeme. Laboratorijske studije su pokazale smanjeni antitrombocitni učinak klopidogrela ako se primjenjuju PPI. Međutim, studije koje se bave kliničkim ishodima su pokazale proturječne rezultate. Nedavni pregledni članak koji je uključio 33 studije pruža vrlo dobar uvid te zaključuje da su klinički podaci vrlo kontradiktorni, ali da čak i novije, bolje dizajnirane studije u bolesnika na klopidogrelu i PPI ne pokazuju dokaze relevantnih nuspojava u pogledu kliničkih ishoda.[52]

Iznenadni srčani zastoj

Iznenadni srčani zastoj je manje rjeđa, ali često fatalna komplikacija AKS. Iako postoje i drugi razlozi za SCA, osobito u mlađih bolesnika, ishemija miokarda je najučestaliji uzrok srčanog zastoja potenciranog malignom tahiaritmijom u bolesnika starijih od 40 godina.[4,37] Većina tih srčanih zastoja se događaju izvan bolnice (izvanbolnički srčani zastoj; OHCA). Preživljavanje bolesnika s OHC je bilo nisko promatrajući posljednjih nekoliko desetljeća, posebice u ruralnim područjima, u prosjeku <10% od ukupnog postotka bolničkog otpusta. Međutim, u posljednjih nekoliko godina preživljavanje je bolje, osobito u metropolitskim područjima. Londonska ambulantna služba je uočila porast stope preživljavanja od 12% do 32% između 2007. i 2012.[5]

Može se samo nagađati o razlozima ovog trenda s obzirom da su se svega nekoliko pojedinačnih postupaka pokazali učinkovitima.[54] Najvjerojatnije se radi o kombinaciji više učinkovitih postupaka koji su odgovorni za uočeno poboljšanje preživljavanja. Rana kompresija prsnog koša i rana defibrilacija su neosporni čimbenici koji značajno mijenjaju ishod.[55] Vjerojatno je da su odigrali glavne uloge dostupnost

95% CI 0.77 to 0.92), and there was also a reduced risk for cardiovascular mortality as a single end point. Overall, there was no significant difference in the rates of major bleeding between the ticagrelor and clopidogrel groups (11.6% vs 11.2%, respectively). However, there was a higher risk of non-coronary artery bypass surgery related major bleeding (4.5% vs 3.8%).

Cangrelor: In contrast to these drugs, cangrelor is administered intravenously. It has been tested against placebo and against clopidogrel. The CHAMPION-PLATFORM trial (placebo control) was stopped early because an interim analysis showed disappointing results. The CHAMPION-PCI trial (clopidogrel as a comparator) failed to show a significant benefit as well. The most recent and largest study, the CHAMPION-PHOENIX trial, compared cangrelor against preloading with 300-600 mg of clopidogrel. This study not only included ACS but also patients with stable CAD. It found a reduced risk for ischaemic events (death, MI, ischaemia-driven revascularisation or stent thrombosis) over the first 48 h without any increase in major bleeding risk[49]. Its role in clinical practice in the context of having ticagrelor and prasugrel available is not clear yet, and it has never been compared against these agents.

With additional and more potent antiplatelet therapies now available, the challenge is to decide which agent to use and when. Currently, the decision is usually based on clinical and risk factors; pharmacogenetics may also play a role in guiding therapies in the future.[50]

Gastrointestinal (GI) bleeding is one of the more common risks of strong antiplatelet therapy. Therefore, PPI are often prescribed as well. A recent study found, interestingly, that lower GI bleeding is more common than upper GI bleeding in patients on PPI.[51] Furthermore, the impact of PPI on the clopidogrel effect has been a matter of controversy for some time. Laboratory studies have suggested a reduced antiplatelet effect if PPI are used. However, studies looking at clinical end points have shown conflicting results. A recent systematic review provides a very good overview, including 33 studies, and concludes that clinical data are highly conflicting but that even newer, better designed studies do not show evidence of a relevant adverse effect of PPI in patients on clopidogrel regarding clinical outcomes.[52]

Sudden Cardiac Arrest

SCA is a less common but often fatal presentation of ACS. While there are other reasons for SCA, especially in younger patients, the most common cause for tachyarrhythmic cardiac arrests in patients over 40 is myocardial ischaemia.[4,37] Most of these cardiac arrests occur out of hospital (out-of-hospital cardiac arrest (OHCA)). Survival for OHCA patients has been poor for several decades, averaging <10% to hospital discharge, and may be even lower, particularly in remote areas. However, in recent years survival has increased, especially in metropolitan areas. The London Ambulance Service observed an increase in survival rates from 12% to 32% between 2007 and 2012.[5]

We can only speculate about the reasons for this improvement since few single interventions have really proven to be effective.[54] It is therefore more likely that it is the combination of multiple effective treatments that is responsible for the observed improvements in survival. Early chest compressions and early defibrillation are the undisputed game changers.[55] It is likely that the availability of public automatic defibrillators, defibrillators of the EMS and public aware-

javno dostupnih automatskih defibrilatora, defibrilatora u HMP i opća svijest te sve veći broj laika obučenih za kompresiju prsnog koša.[56]

Međutim, važni su i drugi čimbenici kao što su terapijska hipotermija i neodgođena angiografija radi definiranja i potencijalnog liječenja osnovnog uzroka.[57,58] Opservacijska studija kod 9.971 bolesnika sa suspektnim srčanim uzrokom OHCA je analizirala ishode s obzirom na bolnicu zbrinjavanja. Bolesnici liječeni u bolnicama s 24-satnom službom intervencijskih kardiologa imali su bolje preživljavanje (OR 1,40, 95% CI 1,12-1,74; p=0,003).

Važeće smjernice preporučuju neodgodivu angiografiju u bolesnika nakon uspješne reanimacije zbog OHCA (povratak spontane cirkulacije) u slučaju elevacije ST-segmenta u postreanimacijskom EKG. Međutim, pouzdanost postreanimacijskog EKG je nejasna i postoje razlozi za preporuku rane angiografije u svih bolesnika preko 35 do 40 godina starosti, bez obzira na EKG, ako ne postoji očiti nekardijalni uzrok.

Rehabilitacija nakon akutnog koronarnog sindroma

Iako se čini intuitivno zaključiti da su programi kardiološke rehabilitacije korisni pružajući pozorno praćenje, nadzor nad fizičkom aktivnošću i pomoć u promjeni načina života, klinički podaci o učincima su kontraverzni.

Nedavno je kardijalna rehabilitacija kod AKS ponovno osporena multicentričnim randomiziranim ispitivanjem RAMIT o kardijalnoj rehabilitaciji u bolesnika nakon akutnog MI.[59] U ovoj studiji, kardijalna rehabilitacije u bolesnika nakon akutnog IM nije imala učinka na mortalitet ili morbiditet, kardiološku terapiju, čimbenike rizika ili promjenu načina života. Moramo spomenuti da je RAMIT istraživanje bilo malo, međutim, ako se detaljno analiziraju dokazi objedinjavanjem svih dostupnih radnomiziranih kontroliranih istraživanja, kao što je učinjeno Cochrane pregledom (kombinirajući 47 studija), postoji značajan, iako skroman učinak na smrtnost.[60] Ova meta-analiza nije uključila rezultate studije RAMIT koji bi dodatno smanjili procijenjeni utjecaj na sveukupnu smrtnost s 13% na 11%.[61] Važno je napomenuti da se Cochrane analiza usredotočila na rehabilitaciju temeljenu na tjelesnim vježbama, pri čemu postoji vjerojatnost da rehabilitacija koja se ne temelji tjelovježbi (edukacija bolesnika) ima mali učinak na smrtnost nakon IM.[62]

Problem s udruživanjem rezultata više istraživanja je, naravno, da to ne uzima u obzir razvitak intervencije.[63] Rezultati novije nerandomizirane kohortne studije OMEGA pokazali su da je kratkoročni sveobuhvatni program kardijalne rehabilitacije nakon akutnog IM znatno poboljšava jednogodišnju prognozu.[64] Bolesnici koji su sudjelovali u rehabilitacijskim programima su imali niži ukupni mortalitet, za razliku od onih koji nisu. Međutim, bez randominizacije interpretacija ovih rezultata je otežana. Postojao je značajan odnos između broja dolaska i učinka; učestalije prisustvovanje je bilo povezano s manjim ukupnim mortalitetom. Međutim, rjeđi polaznici bili su češće pušači i kada su izvršene prilagodbe u pogledu razlika u statusu pušenja, nestao je odnos dolazak-učinak.

Iako kardijalna rehabilitacija kako se trenutno provodi u mnogim zemljama ne može biti učinkovita u smanjenju važnih kliničkih ishoda, još uvijek pomaže u pružanju informacija, savjeta i sigurnosti te dugoročnoj sekundarnoj prevenciji.[65]

ness, and an increasing number of lay people trained in chest compression, played major roles.[56]

However, other factors such as therapeutic hypothermia and immediate angiography to define and potentially treat the underlying cause are important as well.[57,58] An observational study of 9,971 patients with OHCA of suspected cardiac cause were assessed regarding the hospital they were referred to. Those treated at hospitals with 24 h cardiac interventional services had a better survival (OR 1.40, 95% CI 1.12 to 1.74; p=0.003).

Current guidelines recommend immediate angiography in patients after successful resuscitation for an OHCA (return of a spontaneous circulation) in case of ST elevations in the post-resuscitation ECG. However, the accuracy of post-resuscitation ECGs is unclear and there are grounds for recommending early angiography in all patients over 35-40 years, regardless of the ECG, if there is no obvious non-cardiac cause.

Cardiac rehabilitation after ACS

While it seems intuitive that cardiac rehabilitation programmes are beneficial by providing careful follow-up, supervised physical activity and guidance on lifestyle modification, clinical data on its effect are controversial.

Very recently, cardiac rehabilitation for ACS has been challenged again by the multicentre RCT of comprehensive cardiac rehabilitation in patients following acute MI (RAMIT: Rehabilitation After Myocardial Infarction Trial)[59]. In this study, cardiac rehabilitation in patients after an AMI had no effect on mortality or morbidity, cardiac medication, risk factors or lifestyle modification. However, we have to be aware that the RAMIT trial was small and if we look at the evidence more comprehensively, by pooling all available RCTs as done by a Cochrane review (combining 47 studies), there is a significant, albeit modest, effect on mortality[60]. This meta-analysis did not include the RAMIT findings which would have further reduced the estimated effect on all cause mortality from 13% to 11%.[61] It is important to note that the Cochrane review focused on physical exercise based rehabilitation, the probability being that non-exercise based rehabilitation (patient education) has little effect on mortality after MI.[62]

The problem with combining results of multiple trials is, of course, that this does not account for the 'evolution' of such interventions[63]. The results of the recent OMEGA study, which was a non-randomised cohort study, have shown that a short term comprehensive cardiac rehabilitation programme after acute MI significantly improved the 1-year prognosis.[64] Those who attended rehabilitation programmes had lower all-cause mortality than those who did not, but without randomised treatment assignment, interpretation of such data is difficult. There was a significant dose-response relationship; the more sessions attended the lower the all-cause mortality. However, low attenders were more likely to be smokers, and when adjustments were made for baseline differences in smoking status the dose-response association disappeared.

Though cardiac rehabilitation as currently provided in many countries may not be effective in reducing hard clinical end points, it still helps provide information, advice, and reassurance and helps in long term secondary prevention.

Zaključci

Mogućnosti liječenja AKS su se znatno poboljšale u posljednjih nekoliko godina što doprinosi značajnom poboljšanju ishoda. To se posebice odnosi na liječenje STEMI, dok je dugoročni mortalitet nakon NSTE-ACS još uvijek značajan. Uvođenje treće generacije antitrombocitne terapija (prasugrel, tikagrelor) i najnoviji intravenozni oblik, kangrelor, će vjerojatno i dalje poboljšavati kliničke ishode nakon ACS. Ova potentni lijekovi mogu povećati rizik od krvarenja te treba uzeti u obzir povezanost krvarenja i ishoda pa je bitno primjenjivati strategiju izbjegavanja periporceduralnog krvarenja. To može uključivati angiografiju radijalnim pristupom, femoralni pristup vođen ultrazvukom i primjenu bivalirudina.

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Conclusions

The treatment options for ACS have improved significantly over the past few years, contributing to notable improvements in outcomes. This is especially the case for STEMI, while long term mortality after an NSTE-ACS is still considerable. The very recent introduction of third generation antiplatelet therapies (prasugrel, ticagrelor) and the most recent intravenous form, cangrelor, are likely to continue to improve clinical outcomes after ACS. These more potent agents can increase bleeding risks, and considering the association between bleeding and outcomes, periprocedural bleeding avoidance strategies are important. They may include radial access angiography, ultrasound guided femoral access, and the use of bivalirudin.

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