Godina 2020. u kardiovaskularnoj medicini: slikovne tehnike

The year in cardiovascular medicine 2020: imaging

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Uvod

Protekla je godina bila posebna po pandemiji bolesti COVID-19, koja je zahvatila globalnu populaciju, uz teške socioekonomske posljedice. Područje kardiologije također nije bilo pošteđeno, pa su nastale i značajne promjene u svakodnevnom radu. Primjenom različitih slikovnih tehnika ubrzo su prikazane kardiološke manifestacije COVID-a 19, te njihove dijagnostičke i prognostičke implikacije. Još nam uvijek predstoji procjena dugoročnih ishoda praćenja nakon oštećenja miokarda.

Nedavno objavljeni rezultati istraživanja *ISCHEMIA*[1] doveli su do rasprave o ulozi testiranja u bolesnika sa stabilnom koronarnom bolesti srca (CAD), pri čemu dio stručne zajednice misli

Introduction

The past year has been a unique one owing to the outbreak of COVID-19, which has affected the population worldwide, with the ensuing economic and social consequences. The field of cardiology has not escaped this reality bringing with it changes in our everyday clinical praxis. The contribution of different imaging techniques to the cardiac involvement of COVID-19 with diagnostic and prognostic implications has been published very expeditiously. It is still pending to ascertain the long-term outcome of the different degrees of cardiac injury.

The recent publication of the ISCHEMIA trial[1] has resulted in a heated debate on the role of ischaemia testing in patients with stable coro-

da je spomenuto istraživanje dovelo do sankcije ograničene uloge ishemije miokarda u CAD-u. Bilo kako bilo, to nije bio zaključak istraživanja, ni njegova primarna hipoteza, ni dizajn te studije, a ni daljnja ekstrapolacija izvan merituma istraživanja nije bila na mjestu. Slikovne metode za objektivizaciju ishemije i dalje će imati bitnu ulogu u dijagnostici i zbrinjavanju stabilne CAD jer i bolesnici i kardiolozi moraju razjasniti uzrok simptoma kada anatomske promjene u koronarnoj cirkulaciji ne dovode do ishemije niti objašnjavaju simptome, jer bol u prsnom košu može biti i nekoronarnog podrijetla. Nema randomiziranog istraživanja koje bi pokazalo da je slikovni prikaz koronarnih arterija superiorniji u odnosu prema funkcionalnom testiranju. Samo je istraživanje *PROMISE*[2] uspoređivalo dvije navedene strategije i rezultati nisu uputili na bitnije razlike u ishodima u bilo kojemu dijagnostičkom pristupu.

Napredak spoznaja posljedičan primjeni metoda umjetne inteligencije (AI) doveo je do konsolidacije potrebe za većim posvećivanjem pažnje metodi za koju se tijekom nekoliko godina očekuje da postane svakodnevica u rutinskoj kliničkoj praksi. Istaknut ćemo i najnovije preporuke oko primjene slikovnih tehnika u smjernicama za kliničku praksu.

Nakon toga ukratko ćemo prikazati najvažnija istraživanja koja su objavljena u prethodnoj godini, a relevantna su za slikovne metode u suvremenoj kliničkoj praksi (**slika 1**) .

nary artery disease (CAD), with some colleagues advocating that ISCHEMIA has sanctioned the limited role of myocardial ischaemia in patients with stable CAD. However, this is not the conclusion of the trial, nor its primary hypothesis nor the study design and extrapolation beyond these boundaries could be incorrect. Ischaemia imaging will continue to play a major role in the diagnosis and management of stable CAD as both physicians and patients still need to clarify the cause of symptoms, coronary anatomy does not infer ischaemia or explains symptoms, and chest pain can also be of non-coronary origin. Most importantly, there is no randomized trial demonstrating that an imaging approach of coronary anatomy is superior to functional testing. In fact, PROMISE[2] is the only trial that compared the two strategies and it did not demonstrate any difference in outcome between the two approaches.

Furthermore, advances in the knowledge and application of artificial intelligence (AI) are consolidating the need for greater attention and interest regarding a tool that in a few years will become part of our daily clinical practice. Finally, we highlight the introduction of new recommendations in the use of imaging techniques in the new practice guidelines.

We then summarize the most outstanding studies from the last year relating to the most relevant imaging techniques in current cardiology (**Figure 1**).

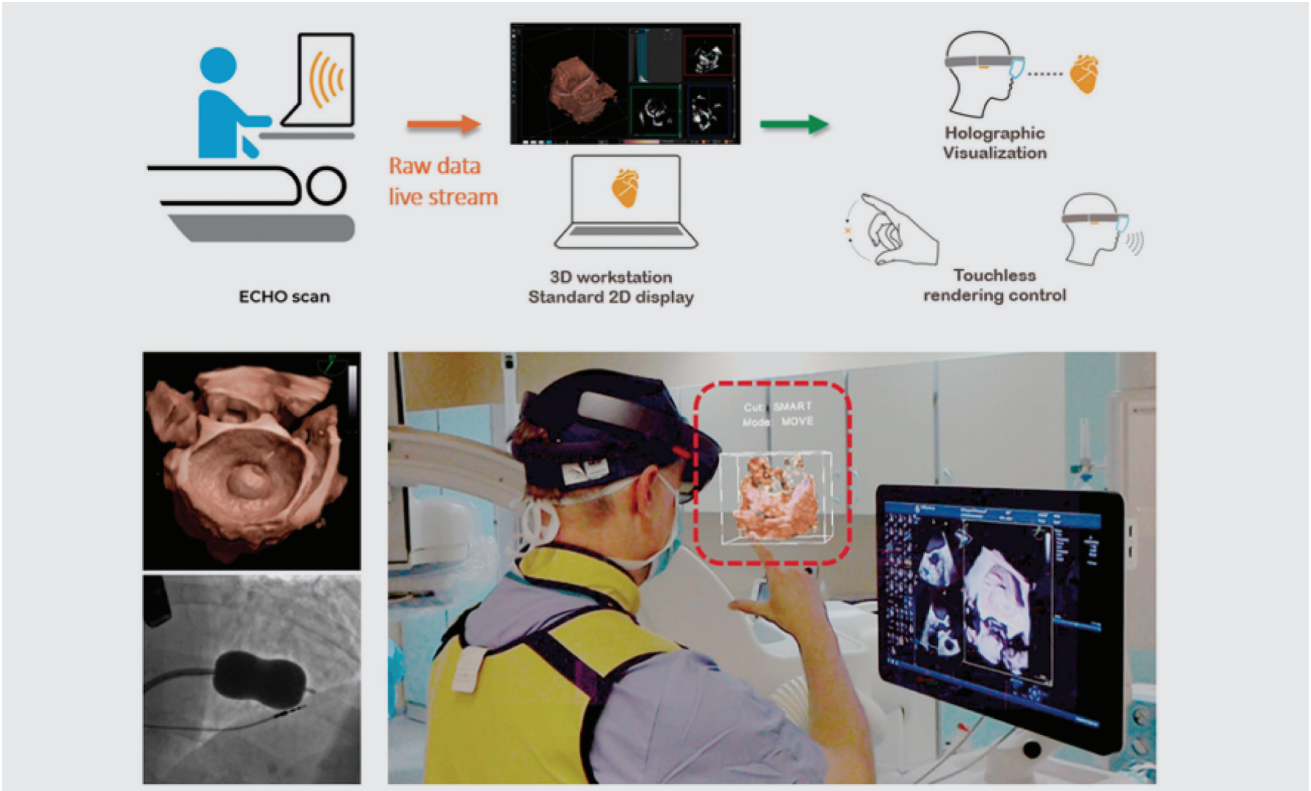

FIGURE 1. Graphical Abstract - Raw 3D data were streamed from standard echocardiograph using custom connection to 3D DICOM viewer workstation (CarnaLife Holo, MedApp, Krakow, Poland) for real-time, dynamic 3D rendering and wirelessly transferred into HoloLensmixed reality display (Microsoft, Redmond, USA) to overlay non-obstructive 3D data hologram upon reality view. Data were visible as a semitransparent holographic cube positioned in a convenient sector of visual field of echocardiographist and shared by interventional cardiologist. Reproduced with permission from Kasprzak et al.[7]

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Ehokardiografija

Ehokardiografija je i dalje klinički najviše primjenjivana metoda za bolje razumijevanje patofiziologije i drugih patoloških ili fizioloških aspekata funkcija srca, te zauzima središnje mjesto u svakodnevnom zbrinjavanju bolesnika. Nekoliko istraživanja objavljeno je u 2020., te ćemo u ovom članku prikazati samo manji udio zaista većeg opsega publikacija iz prethodne godine, vrlo neobične, u kojoj nas je zahvatila pandemija COVID-a 19.

Jedno od polja većeg interesa jest kardiomiopatija u transtiretinskoj amiloidozi (ATTR-CM), koja je prepoznata kao sve učestaliji uzrok popuštanja srca, a uz dostupne nove modalitete liječenja, od kojih su nekima već postignuti zapaženiji klinički uspjesi, njezino prepoznavanje postaje normativ kliničkoga zbrinjavanja. Ehokardiografija je tradicionalno bila uvijek važna za dijagnostiku amiloidoze, a njezina je uloga dodatno osnažena porastom kliničke relevantnosti amiloidoze. Chacko *i sur.*[3] u međunarodnom su registru opisali morfološke i funkcijske tipove kroz spektar divljeg tipa (wtATTR-CM) i nasljedne (hATTR-CM) transtiretinske kardiomiopatije, te ehokardiografskih morfotipova koji su prognostički relevantni. Navedena je grupa uključila 1240 bolesnika s ATTR-CM-om, odnosno 776 s wtATTR-CM-om i 474 hATTR-CM-om, od kojih je 314 imalo varijantu V1221 i 127 varijantu T60A. Pri postavljanju dijagnoze bolesnici s V122I-hATTR-CM-om imali su teži stupanj sistoličke i dijastoličke disfunkcije, uz preostale ehoparametre, a bolesnici s T60A-hATTR-CM-om imali su najmanje iznose odstupanja; bolesnici s wtATTR-CM-om bili su negdje između. Indeks udarnog volumena, indeks površine desnog atrija, longitudinalni *strain* i E/e' bili su neovisno važni za prognozu, te porastom mortaliteta (p<0,05 za sve navedeno). Teška aortalna stenoza (AS) također je bila neovisno povezana s prognozom i s mnogo kraćim preživljenjem (medijan je preživljenja 22 prema 53 mjeseca, p = 0,001). U navedenom istraživanju tri distinktivna genotipa bila su povezana s različitim kliničkim stupnjevima težine. S pomoću ehokardiografije daje se naslutiti o kompleksnim patofiziološkim promjenama sistoličke i dijastoličke funkcije, koje su se pokazale neovisno povezanima s mortalitetom. Koegzistencija teške AS također se pokazala neovisno povezanom sa znatno reduciranim preživljavanjem u bolesnika.

Potreba za definiranjem fizioloških vrijednosti pokazala se vrlo važnom da bi se formirao registar patoloških granica. U tom je smislu istraživanje *NORRE* prikazalo korisne referentne raspone za 2D mjerenja *straina* različitih specifičnih slojeva lijeve klijetke (LV), dobivenih na velikoj grupi zdravih dobrovoljaca iz svih dobnih skupina.[4]

Važnost generiranja parametara koji mogu pomoći za bolje razumijevanje težine pojedinih bolesti, kao i za stratifikaciju rizika u bolesnika od posebne je kliničke vrijednosti. To je posebice slučaj u bolesnika s bikuspidalnim aortalnim zalistkom (BAV). Kong *i sur.*[5] proveli su istraživanje u kojemu su ispitivali udio i prognostičku vrijednost poremećaja globalnoga longitudinalnog *straina* (GLS) LV-a u bolesnika s BAV-om i očuvanom ejekcijskom frakcijom LV-a (LVEF). Ispitivani su udio i prognostička vrijednost poremećaja LV-GLS-a u bolesnika s BAV-om i očuvanom LVEF. Pet stotina trinaest bolesnika s BAV-om i očuvanom LVEF (>50 %) bilo je podijeljeno u 5 grupa na osnovi tipa disfunkcije BAV-a: (i) normalna funkcija BAV-a; (ii) blaga AS ili aortalna regurgitacija (AR); (iii) ≥ umjerena izolirana AS;

Echocardiography

Echocardiography continues to be one of the most used methods to better understand cardiac pathophysiology and different pathological and even normal aspects of cardiac function and also plays a central role in daily patient management. Several papers have been published in 2020, and here, we highlight just a small proportion of the large amount of literature that has been produced during this year, a very unusual one, considering the COVID-19 pandemic that affected all of us.

One area of great current interest is transthyretin amyloidosis cardiomyopathy (ATTR-CM), an increasingly recognized cause of heart failure (HF) and with the new treatment strategies underway, some already with important clinical results; its recognition is becoming a must in clinical scenarios. Echocardiography has always played a role in the diagnosis of amyloidosis and that role is further strengthened with the exponential increase in relevance of amyloidosis. Chacko *et al.*[3] in an international network characterized the structural and functional echocardiographic phenotype across the spectrum of wild-type (wtATTR-CM) and hereditary (hATTR-CM) transthyretin cardiomyopathy and the echocardiographic features predicting prognosis. They studied 1240 patients with ATTR-CM, comprising 766 with wtATTR-CM and 474 with hATTR-CM, of whom 314 had the V122I variant and 127 the T60A variant. At diagnosis, patients with V122I-hATTR-CM had the most severe degree of systolic and diastolic dysfunction across all echocardiographic parameters and patients with T60A-hATTR-CM the least; patients with wtATTR-CM had intermediate features. Stroke volume index, right atrial area index, longitudinal strain, and *E/e'* were independently associated with mortality ($P < 0.05$ for all). Severe aortic stenosis (AS) was also independently associated with prognosis, conferring a significantly shorter survival (median survival 22 vs. 53 months, $P = 0.001$). In this study, the three distinct genotypes presented with varying degrees of severity. Echocardiography indicated a complex pathophysiology in which both systolic and diastolic functions were independently associated with mortality. The presence of severe AS was also independently associated with significantly reduced patient survival.

The need for normal values is very important to set the references to determine the pathological boundaries. In this regard, the NORRE study provided useful reference ranges of 2D echocardiographic measurements of left ventricular (LV) layer-specific strain from a large group of healthy volunteers of both genders over a wide range of ages.[4]

The importance of developing parameters that may help the clinician to better understand the severity of certain disease conditions, as well as risk stratify the patients, is of utmost clinical relevance. That is the case of patients with bicuspid aortic valve (BAV). Kong *et al.*,[5] realized a study to evaluate the proportion and prognostic value of impaired LV global longitudinal strain (GLS) in patients with BAV and preserved LV ejection fraction (EF). It evaluated the proportion and prognostic value of impaired LV GLS in patients with BAV and preserved LVEF. Five hundred and thirteen patients with BAV and preserved LVEF (>50%) were divided into five groups according to the type of BAV dysfunction: (i) normal function BAV, (ii) mild AS or aortic regurgitation (AR), (iii) ≥ moderate

(iv) ≥ umjerena izolirana AR; (v) ≥ umjerene kombinirane AS i AR. Sistolička disfunkcija procijenjena na temelju *2D-speckle tracking* ehokardiografije definirana je kao granična u slučaju kada je LVGLS iznosio –13,6 %. Primarni ishodi istraživanja bili su intervencija na aortalnom zalistku ili ukupna smrtnost. Udio bolesnika s LVGLS-om ≤-13,6 % bio je najviši u bolesnika iz grupe s normalnom funkcijom BAV-a (97 %), a najmanji u skupini s umjerenim i teškim stupnjevima kombinirane AS i AR (79 %). Tijekom medijana praćenja od 10 godina 210 (41 %) bolesnika bilo je podvrgnuto zamjeni aortalnog zalistka, dok je 17 (3 %) bolesnika umrlo. Bolesnici s očuvanom sistoličkom funkcijom (LVGLS ≤–13,6 %) imali su mnogo bolje ishode praćenja do pojave simptoma primarnih ciljeva u usporedbi s onima koji su imali oštećenu funkciju lijeve klijetke (LVGLS >–13,6%). Poremećaj vrijednosti LVGLS-a kod BAV-a pokazao se neovisno povezanim s povećanim rizikom od pojave kliničkih događaja (uglavnom zamjene aortalnog zalistka): *hazard ratio* (HR) 1,09; P< 0,001. Na temelju navedenog poremećaj LVGLS-a u BAV-u uz očuvanu sistoličku funkciju nije bio rijedak, a bio je znatno neovisno povezan s povećanim rizikom od neželjenih kliničkih događaja.

Vrijednost GLS-a značajan je prediktor neželjenih kardiovaskularnih ishoda u osoba muškog spola. Istraživanja su pokazala da GLS nije toliko pouzdan za pretkazivanje neželjenih ishoda u osoba ženskoga spola. Lundorff *i sur.*[6] identificirali su ehokardiografske prediktore kardiovaskularnog morbiditeta i mortaliteta u 1245 žena iz opće populacije, bez pojave HF-a i fibrilacije atrija, koje su obavile ehokardiografski pregled koji je uključivao tkivni dopler. Od toga je 747 žena imalo dostupnu analizu *straina*. Primarni cilj istraživanja uključivao je zajednički ishod, od akutnog infarkta miokarda (IM), HF-a i kardiovaskularne smrtnosti. Tijekom praćenja (medijan 12,5 godina) u 162 žene (13,0 %) registriran je primarni zajednički ishod. Te su žene imale viši indeks mase lijeve klijetke (LVMI), učestaliju hipertrofiju LV-a, niži E/A, viši E/e', veće dimenzije LV-a i dulje deceleracijsko vrijeme. LVMI i e' ostali su važni prognostički čimbenici zajedničkog ishoda. GLS nije bio neovisni pretkazatelj ishoda nakon multivarijatne prilagodbe. Autori su zaključili da su stupanj hipertrofije LV-a, procijenjen kao LVMI, i dijastolička disfunkcija procijenjena s pomoću e' bili povezani s neželjenim kardiovaskularnim događajem u žena u općoj populaciji.

Neke tehnološke inovacije u ehokadiografiji također se napominju u nekoliko kratkih izvješća, poput razvoja 3D prijenosa transezofagusnih ultrazvučnih podataka u stvarnome vremenu u holografski vizir koji se nosi na glavi, te omogućuju dijeljenje podataka s kateterizacijskim laboratorijem. Ta je metoda prvobitno iskušana u ljudi tijekom perkutane mitralne balonske komisurotomije[7]. U drugoj je publikaciji prezentirana nova metoda fuzije 3D ehokardiografije i magnetne rezonancije (MR) u vremenu (sredina dijastole) i prostoru primjenom novog algoritma na temelju oznaka i sekundarnog spajanja obiju slika koje omogućuju segmentaciju za 3D printanje. Spomenuti je produkt prikazan u djevojčice s VSD-om i mobilnim mitralnim zalistkom nakon operacije arterijske zamjene[8].

Drugo važno istraživanje koje je ispitivalo primjenu umjetne inteligencije u kardiovaskularnom oslikavanju objavili su Ghorbani *i sur.*[9], a ispitivalo je model (*Echonet*) razvoja dubokog učenja. Nakon treninga s 2,6 milijuna ehokardiograma model je bio sposoban mjeriti s dobrom pouzdanošću različite srčane strukture i volumene LV-a u terminalnoj sistoli i dijastoli (R2 = 0,74 i R2 = 0,70), EF (R2 = 0,50), povećanje LA-a i

isolated AS, (iv) ≥ moderate isolated AR, and (v) ≥moderate mixed AS and AR. LV systolic dysfunction based on 2D speckle-tracking echocardiography was defined as a cut-off value of left ventricular global longitudinal strain [LVGLS (–13.6%)]. The primary outcome was aortic valve intervention or all-cause mortality. The proportion of patients with LVGLS ≤–13.6% was the highest in the normal BAV group (97%) and the lowest in the group with moderate and severe mixed AS and AR (79%). During a median follow-up of 10 years, 210 (41%) patients underwent aortic valve replacement and 17 (3%) died. Patients with preserved LV systolic function (LVGLS ≤–13.6%) had significantly better event-free survival compared to those with impaired LV systolic function (LVGLS >–13.6%). LVGLS was independently associated with increased risk of events (mainly aortic valve replacement): hazard ratio (HR) 1.09; $P < 0.001$. Therefore, impaired LVGLS in BAV with preserved LVEF is not infrequent and was independently associated with increased risk of events.

GLS is a strong predictor of adverse cardiovascular outcome in men. However, studies have indicated that GLS may not predict cardiovascular outcomes as effectively in women. Lundorff *et al.*[6] identified echocardiographic predictors of cardiovascular morbidity and mortality in 1245 women from the general population free of HF and atrial fibrillation, who had an echocardiographic examination performed including tissue Doppler imaging. In this subset, 747 women had images eligible for strain analysis. Endpoint was a composite of acute myocardial infarction (MI), HF, and cardiovascular death. During follow-up (median 12.5 years), 162 women (13.0%) reached the composite outcome. These women had higher LV mass index (LVMI), more LV hypertrophy, lower *E/A*, higher *E/e'*, larger LV dimensions, and longer deceleration time. LVMI and e' remained as significant predictors of the composite outcome. GLS was not an independent predictor of outcome after multivariable adjustment. The authors concluded the degree of LV hypertrophy assessed as LVMI and diastolic dysfunction evaluated by *e'* were associated with adverse cardiovascular outcome in women from the general population.

Some new technological developments in echocardiography have also been described in some short papers, such as the development of a method of real-time streaming of 3D-transesophageal echocardiography data into head-mounted mixed-reality holographic display allowing for touchless control and data sharing within the cath-lab. The method was tested for the first time in human during percutaneous mitral balloon commissurotomy.[7] In another paper, it was presented a novel fusion pipeline that first aligns 3D echocardiography and magnetic resonance imaging (MRI) in time (mid-diastole) and space using a landmark-based registration algorithm and second fuses both images enabling combined image segmentation for 3D printing. This pipeline was demonstrated in young girl with VSD and straddling mitral valve after an arterial switch operation.[8]

Another outstanding study exploring the use of artificial intelligence in cardiac imaging is that of Ghorbani *et al.*[9] in which a model (Echonet) of deep learning is developed. After training with 2.6 million echocardiograms the model is capable of measuring with good accuracy different cardiac structures and function such as LV end systolic and diastolic volumes (R2 = 0.74 and R2 = 0.70), EF (R2 = 0.50), left atrial enlargement, and LV hypertrophy. Moreover, like other

hipetrofiju LV-a. Nadalje, poput ostalih modela AI, *Echonet* je bio sposoban identificirati fenotipove dobi (R2 = 0,46), spola (AUC = 0,88), težine (R2= 0,56) i visine (R2= 0,33), koje ehokardiografičar teško može sam razaznati. Uz činjenicu da je ehokardiografija najčešće primjenjivana dijagnostička metoda u kardiologiji, bez značajnijih polemika i prilično široko dostupna, čini se da se s pomoću metoda AI može smanjiti potreba za ljudskim resursima pri interpretaciji slika, te time učiniti ultrazvuk dostupniji općoj populaciji. Nadalje, mogli bi se stvoriti prediktivni modeli kardiovaskularnih događaja na temelju parametara koji su teško dostupni ljudskoj svijesti.

Naposljetku, u posljednjim objavljenim smjernicama ističemo da je ehokardiografija uključena u I. razred preporuka, demonstrirajući relevantnost metode u rutinskoj kardiološkoj praksi.[10-13]

Magnetna rezonancija srca

U posljednjoj godini magnetna rezonancija srca (CMR) potvrdila je ulogu u dijagnostici, zbrinjavanju i prognostičkim analizama bolesnika s bolima u prsnom košu, kod ishemijske bolesti srca i neishemijskih kardiomiopatija, s pomoću metoda AI i strojnog učenja (ML).

Istraživanje *MR-INFORM* nemaskirana je multicentrična studija kliničke učinkovitosti u bolesnika s tipičnom anginom čije je zbrinjavanje randomizirano u grupu na strategiji CMR perfuzijskog oslikavanja ili grupu analize frakcije protoka (FFR).[14] Primarni zajednički ishod, od smrtnosti, nefatalnog infarkta miokarda ili revaskularizacije klinički značajne lezije unutar 1 godine, dogodio se u 15 od 421 bolesnika (3,7%) u FFR grupi [razlika rizika, −0,2 postotna boda; 95 %-tni interval pouzdanosti (CI) −2,7 − 2,4], demonstrirajući neinferiornost stresnog CMR-a prema FFR-u u pogledu neželjenih kliničkih događaja. Stresni CMR rezultirao je manjom učestalosti incidencije koronarnih revaskularizacija nego FFR.

Stresni perfuzijski CMR pokazao se kao izvrsna dijagnostička i prognostička metoda u monocentričnoj američkoj studiji (*SPINS*).[15] Bolesnici bez znakova ishemije i bez kasne imbibicije gadolinijem (LGE) s pomoću CMR-a (n = 1583, 67 %) imali su nisku stopu primarnih neželjenih kardiovaskularnih događaja u smislu kardiovaskularnog mortaliteta ili nefatalnog infarkta miokarda (<1 %) i koronarne revaskularizacije (1 − 3 %). Suprotno tomu, bolesnici s ishemijom i LGE-om imali su više od 4 puta uvećanu godišnju stopu neželjenih događaja i više od deseterostruko uvećanu stopu revaskularizacija u prvoj godini nakon CMR-a. Implicira se da bolesnici bez ishemije i bez LGE-a na CMR-u imaju nisku učestalost neželjenih kardiovaskularnih događaja, malu potrebu za revaskularizacijskim liječenjem i male troškove dijagnostike ishemije. Troškovna učinkovitost istraživanja SPINS pokazala je da stresni CMR može biti troškovno učinkovita metoda za izbjegavanje invazivne koronarografije (ICA) u bolesnika s rizikom od opstruktivne CAD.[16] Posebice porast stope troškovne učinkovitosti za strategiju koja u osnovi ima CMR u usporedbi s neslikovnom strategijom iznosi 52 000 USD/kvalitetno provedenih godina života (QALY), dok je porast troškovne učinkovitosti za neposrednu ICA bio 12 milijuna USD/QALY, kada je usporedimo s CMR-om.

Nedavno razvijena metoda kvantitativne CMR stresne perfuzije s automatskim mjerenjima metodama AI[17] validirana je klinički.[18] Napredak u mogućnostima snažnih kompjutorskih

AI models, Echonet is capable to identify phenotypes of age (R2 = 0.46), sex (AUC = 0.88), weight (R2 = 0.56), and height (R2 = 0.33) difficult to assess by human evaluation. Considering that echocardiography is the most widely used imaging test in cardiology, it is anodyne and quite accessible; having the support of AI could reduce the need for human resources in the interpretation of the images allowing the study to be offered to a broader population. Furthermore, it could generate predictive models of cardiovascular events by identifying parameters that are difficult to evaluate by humans.

Finally, in the latest published guidelines, we have appreciated the inclusion of echocardiography with class I recommendation, reflecting the relevance of this technique in routine cardiology practice.[10–13]

Cardiovascular magnetic resonance

Over the last year, cardiovascular magnetic resonance (CMR) has confirmed an established role in the diagnosis, management, and prognosis of patients with chest pain, ischaemic heart disease, and non-ischaemic cardiomyopathies, further improved by AI and machine learning (ML).

The MR-INFORM trial is an unblinded, multicentre, clinical-effectiveness trial in patients with typical angina whose management was randomly assigned to a CMR stress perfusion-based strategy or an fractional flow reserve (FFR)-based strategy.[14] The primary outcome of death, non-fatal MI, or target-vessel revascularization within 1 year occurred in 15 of 421 patients (3.6%) in the cardiovascular MRI group and 16 of 430 patients (3.7%) in the FFR group [risk difference, −0.2 percentage points; 95% confidence interval (CI) −2.7 to 2.4], demonstrating the non-inferiority of stress CMR to FFR with respect to major adverse cardiac events. Stress CMR was also associated with lower incidence of coronary revascularisation than FFR.

The Stress CMR Perfusion Imaging in the United States (SPINS) study demonstrated excellent diagnostic and prognostic value of stress CMR in single-centre study.[15] Patients with no ischaemia or late gadolinium enhancement (LGE) by CMR (*n* = 1583, 67%) experienced low annualized rates of primary outcome of cardiovascular death or non-fatal MI (<1%) and coronary revascularization (1–3%). In contrast, patients with ischaemia and LGE experienced a more than four-fold higher annual primary outcome rate and a >10-fold higher rate of coronary revascularization during the first year after CMR. The implication is that patients without ischaemia or LGE on CMR have a low incidence of cardiac events, little need for coronary revascularization, and low spending on subsequent ischaemia testing. The cost-effectiveness study of SPINS demonstrated that, stress CMR can be a cost-effective gatekeeping tool prior to invasive coronary angiography (ICA) in patients at risk for obstructive CAD.[16] In particular, the incremental cost-effectiveness ratio for the CMR-based strategy compared with the no-imaging strategy was $52 000/quality-adjusted life years (QALY), whereas the incremental cost-effectiveness ratio for the immediate ICA strategy was $12 million/QALY compared with CMR.

Recent developments on quantitative CMR stress perfusion with automated measurements using AI[17] have been validated clinically.[18] The advances in computation power permit inline automated annotation and the use sophisticated myocardial

kalkulacija omogućuje neposrednu automatizaciju i primjenu sofisticiranih metoda perfuzije (npr. model izmjene krv-tkivo) da se riješe uz malu varijabilnost u stvarnom vremenu tijekom oslikavanja, nasuprot satima kompleksnih analiza s varijabilnim rezultatima.

Knott *i sur.* ispitivali su prognostičku važnost ove nove tehnologije u 1049 bolesnika s poznatom ili suspektnom CAD te su reducirani protok kroz miokard (MBF) i perfuzijska rezerva miokarda (MPR) automatski kvantificirani bili snažni neovisni prediktor neželjenih kardiovaskularnih ishoda. Za svaki 1 mL/g/min pada u stresni MBF, korigirani HR za smrt i veliki kardiovaskularni događaj (MACE) bili su 1,93 (95 % CI 1,08 – 3,48; P = 0,028), odnosno 2,14 (95% CI 1,58–2,90; P < 0,0001), čak i nakon prilagodbe za dob i komorbiditete.[19]

Metode AI i ML čine nam dostupnim mogućnosti i otvaraju novo polje kardiovaskularnog oslikavanja s bržim i boljim analizama slika. *Bhuva i sur.*[20] provodili su multicentrično, humano ML CMR istraživanje da se ispita reproducibilnost preciznosti oslikavanja kardiološkim biomarkerima. Preciznost kalkulacije LVEF-a u 110 bolesnika s različitim oblikom bolesti, iz multiplih institucija i s pomoću skenera različitih proizvodnji, kao i različitih snaga polja bile su podjednake kod eksperata, treniranih početnika i automatiziranih mjerenja [koeficijent varijacije 6,1 (5,2 – 7,1 %), P = 0,2581; 8,3 (5,6 – 10,3 %), P = 0,3653; 8,8 (6,1–11,1%), P = 0,8620]. Automatizirana analiza bila je 186 puta brža nego u ljudi (0,07 *vs.* 13 min). Zaključeno je da je automatizirana ML analiza mnogo brža, uz podjednaku preciznost kao kod zdravstvenih djelatnika eksperata.

Porast primjene AI u postprocesuiranju i analizi slika CMR-a dovodi do poboljšanja preciznosti mjerenja, pa točnost i pouzdanost postaju manje ovisne o iskustvu djelatnika. To može imati neposredne implikacije na manje iskusne centre za izvođenje CMR-a, odnosno povećavaju dostupnost CMR-a. Nadalje, poboljšana dijagnostika također je u paru s brzom analizom slike koja se prenosi u poboljšanom vremenu do liječnika, kao atraktivna inačica za vremenski limitirane rasporede rada.

U 30 – 40 % bolesnika s resinkronizacijskom terapijom (CRT) ne uspijeva se postići dovoljno uspjeha, te je potrebno identificirati načine za bolju selekciju bolesnika. U prospektivnom multicentričnom istraživanju provedenom u 200 bolesnika s CRT-om, Aalen *i sur.* pokazali su da kombinacija funkcije lateralne stijenke i septuma, mjerena radom miokarda unutar *pressure-strain* analize na ehokardiografiji i ožiljka miokarda s pomoću CMR LGE-a može ponuditi precizan i relativno jednostavan alat da se poboljša selekcija kandidata za CRT, osobito u bolesnika s ishemijskom kardiomiopatijom i/ili umjerenim trajanjem kompleksa QRS-a. Odgovor na CRT može se predvidjeti razlikom rada između lateralne stijenke i septuma s vrijednostima površine ispod krivulje (AUC) od 0,77 (95 % CI 0,70 – 0,84). Kombinacija septalne vijabilnosti s pomoću CMR-a i razlike rada miokarda na ehokardiografiji znatno je povisila predviđeni odgovor na terapiju CRT-om terapiju dovodeći do porasta krivulje; AUC od 0,88 (95 % CI 0,81 – 0,95).[21]

Uloga CMR-a u dijagnozi amiloidoze srca (CA) postaje sve važnija. Jedna od najvažnijih tehničkih dostignuća u protekloj godini je demonstracija da novi alat koji se naziva tenzorom difuzije miokarda (DT-CMR) može karakterizirati mikrostrukturne učinke deponiranja infiltrata amiloida u bolesnika. Khalique *i sur.* pokazali su da ova beskontrastna tehnika i bez primjene ionizacijskog zračenja može identificiperfusion models (e.g. the blood-tissue exchange model) to be solved with low variability in real time during scanning vs. hours of complex analysis with potentially variable results.

Knott *et al.* assessed the prognostic significance of this new technology in 1 049 patients with known or suspected coronary artery disease reduced myocardial blood flow (MBF) and myocardial perfusion reserve (MPR) quantified automatically inline were strong independent predictors of adverse cardiovascular outcome. For each 1 mL g^{-1} min^{-1} decrease in stress MBF, the adjusted HRs for death and major cardiovascular event (MACE) were 1.93 (95% CI 1.08–3.48; *P* = 0.028) and 2.14 (95% CI 1.58–2.90; *P* < 0.0001), respectively, even after adjusting for age and comorbidities.[19]

AI and ML are providing new opportunities and pushing the envelope in cardiovascular imaging on faster better image analysis. Bhuva *et al.*[20] conducted a multicentre, human and ML CMR study to test generalizability and precision in imaging biomarker analysis. The precision in calculating LVEF in 110 patients with a range a disease, multiple institutions, and different scanner manufacturers and field strengths were similar among expert, trained junior, and automated [coefficient of variation 6.1 (5.2–7.1%), *P* = 0.2581; 8.3 (5.6–10.3%), *P* = 0.3653; 8.8 (6.1–11.1%), *P* = 0.8620]. However, the automated analysis was 186 times faster than humans (0.07 vs. 13 min), concluding that automated ML analysis is faster with similar precision to the most precise (expert) human assessment.

The increasing use of AI in CMR post-processing and image analysis is improving measurements' precision, accuracy and reliability which become less dependent on operator's experience. This can have the direct consequence of empowering less-experienced centres to perform CMR, thus increasing CMR availability. Moreover, the improved diagnostics is also coupled with rapid image analysis which translated in improved physician time of efficiency, an attracting feature for busy clinical schedules.

Up to 30–40% of patients undergoing cardiac resynchronization therapy (CRT) show no improvement, and there is a necessity to improve the selection of patients. In a prospective multicentre study of 200 CRT recipients, Aalen *et al.* demonstrated that the combination of septal and lateral wall function measured by myocardial work with pressure-strain analysis on echocardiography and myocardial scar assessed by CMR LGE can offer a precise and relative simple approach to improve selection of CRT candidates, particularly in patients with ischaemic cardiomyopathy and/or intermediate QRS complex (QRS) duration. CRT response was predicted by the work difference between septum and lateral wall with an area under the curve (AUC) of 0.77 (95% CI 0.70–0.84). The combination of septal viability by CMR combined with myocardial work difference assessment significantly increased predicted CRT response reaching an AUC of 0.88 (95% CI 0.81–0.95).[21]

The role of CMR in the diagnosis of cardiac amyloidosis (CA) is becoming increasingly established. One of the most impactful technical developments this year is the demonstration that a novel approach called diffusion tensor CMR (DT-CMR) can characterize the myocardial microstructural effects of amyloid infiltration in patients. Khalique *et al.* showed that this contrast-free and radiation-free technique can identify the location and extent of the expanded disorganized myocardium. Moreover, novel imaging biomarkers of

rati lokalizacije i stupanj proširenosti ekspandiranoga disorganiziranog miokarda. U skladu s tim, novi slikovni biomarkeri difuzivnosti i frakcionalne anizotropije mogu učinkovito razlikovati CA (n = 20) od hipertrofične kardiomiopatije (HCM; n = 11). Preliminarni rezultati ove inovativne *in vivo* tehnike upućuju na nove patofiziološke mehanizme i poboljšanu dijagnostiku, pružajući obećavajuće nove dimenzije u procjeni poremećaja srčanog mišića.[22]

Registar hipertrofičnih kardiomiopatija (Registar HCMR) uključio je 2755 bolesnika s HCM-om iz 44 centra u 6 država, a uključuje CMR, genske i podatke biomarkera kako bi se poboljšala predikcija rizika. Osnovni podatci identificiraju 2 podskupine bolesnika: grupu s pozitivnim mutacijama sakromera i većom fibrozom na CMR te grupu s negativnim mutacijama sarkomera i manjom fibrozom.[23] Grupa koja je bila pozitivna na mutacije sarkomera i veću fibrozu imala je manju opstrukciju u mirovanju, dok je druga grupa imala više izoliranu bazalnu septalnu hipertrofiju i opstrukciju. Stupanj opstrukcije čini se važnim obilježjem za razlikovanje tih dviju grupa.

U unicentričnoj studiji Raman *i sur.*[24] ispitivali su mehanizme progresije fibroze u bolesnika s HCM-om. Porast LGE-a je bio znatan u onih s poremećenim MPR <1,40 i energijom (fosfokreatin/adenozin trifosfat) na početnom CMR-u (P ≤ 0,01 za oboje). Značajna progresija u LGE-u bila je povezana sa stanjenjem LV, dilatacijom LV i reduciranom sistoličkom funkcijom, te je dovela do peterostruko povećanog rizika od neželjenih kliničkih događaja (HR 5,04, 95 % CI 1,85 – 13,79; P = 0,002).

Od početka pandemije COVID-a 19 porastao je broj publikacija o ulozi CMR-a u detekciji lezije miokarda u oboljelih. Dok CMR ima jasnu kliničku ulogu u identifikaciji lezije kardiomiocita u bolesnika s različitim kardiovaskularnim bolestima, istraživanja o ulozi CMR-a u bolesnika s COVID-om 19 do sada (u trenutku pisanja ovog članka) još su uvijek preliminarna. Potvrda rezultata očekuje se iz velikih multicentričnih istraživanja prije negoli se može predložiti klinička primjena. U opservacijskom monocentričnom njemačkom istraživanju[25] koje opisuje CMR nalaz u 100 asimptomatskih bolesnika koji su se nedavno oporavili od COVID-a 19 (>2 tjedna od postavljanja dijagnoze i nestanka respiratornih simptoma te negativizacije na testiranju brisom na kraju izolacijskog razdoblja), od kojih je 67 bilo liječeno kod kuće (n = 18 asimptomatskih; n = 49 blagi do umjereno teški simptomi), a samo je n = 33 bolesnika zbog težine simptoma trebalo hospitalizaciju. Kohorta je uspoređena s 50 zdravih kontrola, bez čimbenika rizika. Pokazano je da 78 bolesnika (78 %) ima poremećen nalaz CMR-a, uključujući nativni T1 (n = 73), porast nativnog T2 (n = 60), prisutnost LGE (n = 32) ili prisutnost kontrastnog pojačanja perikarda (n = 22). U vrijeme CMR-a visokosenzitivni troponin T (hs TnT) bio je detektabilan (>3 pg/mL) u 71 bolesnika koji su se nedavno oporavili od COVID-a 19, a znatno povišen (>13,9 pg/ML) u 5 bolesnika (5 %). Uspoređujući sa zdravim kontrolama bez rizika, bolesnici koji su se nedavno oporavili od COVID-a 19 imali su manju LVEF, veći volumen LV, te više vrijednosti nativnih T1 i T2. Dok su rezultati široko opisanih varijacija promjena na srcu s pomoću CMR-a u asimptomatskih bolesnika prethodno zaraženih SARS-CoV-2 virusom intrigantni, kliničko značenje tih nalaza nije jasno i još uvijek treba vremena da se odredi. Nažalost, rezultati su spomenutog istraživanja prenaglašeni i dijelom senzacionalistički prihvaćeni od medija, stvarajući zabrinutost u javno-

diffusivity and fractional anisotropy can effectively discriminate CA (n = 20) from hypertrophic cardiomyopathy (HCM) (n = 11). The preliminary results of this innovative in vivo technique suggest novel pathophysiological mechanisms and improved diagnostics, proving a promising new dimension in the assessment heart muscle disorders.[22]

The Hypertrophic Cardiomyopathy Registry (HCMR Registry) recruited 2755 patients with HCM from 44 sites in 6 countries, and includes CMR, genetic, and biomarkers data in order to improve risk prediction. The baseline data identified two distinct subgroups of patients: a group with sarcomere positive mutation and more fibrosis by CMR and a group sarcomere mutation negative with less fibrosis.[23] The group that was sarcomere mutation positive and more fibrosis had less resting obstruction, whereas the other group had more likely isolated basal septal hypertrophy with obstruction. The degree of obstruction appears an important feature that differs between the two groups.

In a single-centre study, Raman *et al.*[24] investigated the mechanisms of fibrosis progression in patients with HCM. LGE increment was significantly higher in those with impaired MPR < 1.40 and energetics (phosphocreatine/adenosine triphosphate) <1.44 on baseline CMR ($P \leq 0.01$ for both). Substantial LGE progression was associated with LV thinning, LV dilatation, and reduced systolic function and conferred a five-fold increased risk of subsequent clinical events (HR 5.04, 95% CI 1.85–13.79; P = 0.002).

Since the beginning of the COVID-19 pandemic, there are an increasing number of publications on the role of CMR in detecting myocardial damage in infected individuals. Whilst CMR has a clear clinical role in identifying cardiac damage in patients with a range of cardiovascular disease, the results of the CMR studies in COVID-19 patients to date (at the time of writing this manuscript) are still preliminary. Confirmatory results are warranted from large-scale multicentre studies with robust methodology before change in clinical management can be advocated. Most notably, an observational single-centre study in Germany[25] describes the CMR findings in 100 asymptomatic patients recently recovered from the COVID-19 infection (>2 weeks from original diagnosis and resolution of the respiratory symptoms and negative results on a swab test at the end of the isolation period) of whom n = 67 recovered at home (n = 18 asymptomatic, n = 49 minor-to-moderate symptoms) and only n = 33 with severe symptoms requiring hospitalization. The cohort was compared to 50 healthy and risk factor-matched controls. They showed that 78 patients (78%) had abnormal CMR findings, including raised myocardial native T1 (n = 73), raised myocardial native T2 (n = 60), presence of myocardial LGE (n = 32), or presence of pericardial enhancement (n = 22). At the time of the CMR, high-sensitivity troponin T (hsTnT) was detectable (>3 pg/mL) in 71 patients recently recovered from COVID-19 (71%) and significantly elevated (>13.9 pg/mL) in 5 patients (5%). Compared with healthy controls and risk factor-matched controls, patients recently recovered from COVID-19 had lower LVEF, higher left ventricle volumes, and raised native T1 and T2. Whilst the results of widespread cardiac changes detected by CMR in asymptomatic patients previously infected by the SARS-CoV-2 virus are intriguing, the clinical significance of these findings is unclear and still needs to be determined. Unfortunately, the results of this study have been overemphasized, and in part

sti, zbunjenost u liječničkog osoblja i skepticizam kod stručne javnosti koja se bavi kardiovaskularnom slikovnom dijagnostikom. U tijeku su multicentrična prospektivna istraživanja koja obuhvaćaju veći broj bolesnika u svrhu otkrivanja i mjerenja akutnih i kroničnih oblika kardijalne lezije uz COVID-19, npr. COVID-heart i COVID-PHOSP.

Sve je više preporuka o primjeni CMR-a u dijagnostici i liječenju bolesnika s kardiovaskularnim bolestima. U posljednje Smjernice ESC-a za zbrinjavanje akutnoga koronarnog sindroma u bolesnika bez perzistentne ST-elevacije iz 2020.[12] prvi put je uključen CMR u obliku preporuke I. razreda, stupanj dokaza B, kod svih bolesnika s IM-im i neopstruktivnom CAD bez jasnog čimbenika.

Kompjutorizirana tomografija

Nova istraživanja u području primjene kompjutorizirane tomografije (CT) u kontekstu kardiovaskularnih (CV) bolesti istaknula su njezinu mogućnost predikcije CV događaja, kao i terapijske smjernice u primarnoj prevenciji.

Nedavno objavljeno istraživanje *ROBINSCA* proučavalo je učinkovitost probira CV bolesti u asimptomatskih ispitanika, koristeći se SCORE modelom (n = 12 185) ili izračunom koronarnoga arterijskog kalcija (CAC) (n = 12 959). Obje su skupine podijeljene u nizak, umjeren ili visok rizik, 10-godišnji rizik od razvoja fatalnih i nefatalnih CV događaja. Skupina s primijenjenim SCORE modelom identificirala je 45,1 % ispitanika niskog rizika (SCORE <10 %), 26,5 % umjerenog rizika (10 – 20 %), te 28,4% visokog rizika (≥20 %). Prema CAC probiru, 76,0 % ispitanika bilo je niskog rizika (Agatson <100), 15,1 visokog rizika (100 – 399), te 8,9 % vrlo visokog rizika (≥400). Probir primjenom CAC-a znatno je reducirao udio ispitanika koji su zahtijevali preventivno liječenje u usporedbi s SCORE-om (relativna redukcija: žene 37,2 %; muškarci 28,8 %).[26]

U multicentričnom istraživanju *CAC Consortium* 66 636 asimptomatskih bolesnika analizirano je CT-om primjenom multivarijatnoga regresijskog modela radi analize ukupne smrtnosti i specifične smrtnosti, i to na osnovi vrijednosti CAC-a. Nakon prilagodbe osobe s CAC-om ≥1000 imale su 5,04, 6,79, 1,55 i 2,89 puta veći rizik od CV bolesti, CAD-a, maligne bolesti te ukupne smrtnosti, u usporedbi s onima koji su imali vrijednost 0. Skupina s CAC-om ≥1000 imala je 1,71, 1,84, 1,36 i 1,51 puta povišeni rizik od CV bolesti, CD-a, maligne bolesti te od ukupne smrtnosti u usporedbi s onima koji su imali vrijednost 400 – 999. Ovo vodi razmatranju agresivnijih modela preventivnih strategija za bolesnika s vrijednostima CAC-a ≥1000.[27]

U istraživanju *MESA* razmatrana je vrijednost CAC-a za primjenu acetilsalicilatne kiseline u primarnoj prevenciji. Svi sudionici (n = 6470) podvrgnuti su temeljnoj procjeni vrijednosti CAC-a. Kardiovaskularni je rizik procijenjen primjenom sjedinjene kohortne jednadžbe (PCE), definirajući tri kategorije rizika: <5 %, 5 – 20 % i >20 %. Na temelju PCE-a broj bolesnika koje je potrebno liječiti u 5 godina (NNT5) bio je veći ili podjednak broju potrebnom za škodljivo djelovanje tijekom 5 godina (NNH5), među svim trima CV kategorijama rizika. Obrnuto, vrijednosti CAC-a ≥100 i CAC ≥ 400 identificirane su kao podgrupe u kojima je NNT5 bio niži od NNH5. Ovo je oboje bilo potvrđeno (za CAC ≥100, NNT5 = 140 *vs.* NNH5 = 518) unutar svih triju kategorija rizika. Također je CAC = 0 identificirao podgrupu u kojoj je NNT5 mnogo veći od NNH5.[28]

sensationalized, by the media with the inevitable results of creating concerns among members of the public, confusion among physicians, and a degree of scepticism among imaging experts internationally. Multicentre large-scale prospective CMR studies to detect and measure acute and chronic cardiac damage of the COVID-19 infection are currently underway, COVID-Heart and COVID-PHOSP among others.

The recommendations for the use of CMR in the diagnosis and management of patients with cardiovascular disease are increasing. In the latest release of ESC guidelines in 2020, the Guidelines for the Management of Acute Coronary Syndromes in Patients Presenting without Persistent ST-segment Elevation[12] includes for the first time CMR as a class I recommendation, level of evidence B in all patients with MI and unobstructed coronary arteries without an obvious cause.

Computed tomography

Over the past year, studies concerning computed tomography (CT) in the cardiovascular scenario have strengthened its ability as a predictor of cardiovascular events, and as a therapeutic guide in primary prevention.

Recently, ROBINSCA trial assessed the effectiveness of cardiovascular disease (CVD) screening in asymptomatic participants using the SCORE model (*n* = 12 185) or coronary artery calcium (CAC) scoring (*n* = 12 950). Both arms were stratified into low, intermediate, or high 10-year risk for developing fatal and non-fatal cardiovascular disease. SCORE screening arm identified 45.1% at low risk (SCORE <10%), 26.5% at intermediate risk (10–20%), and 28.4% at high risk (≥20%). According to the CAC screening, 76.0% were at low risk (Agatston <100), 15.1% at high risk (100–399), and 8.9% at very high risk (≥400). CAC scoring significantly reduced the proportion of individuals needing preventive treatment compared to SCORE (relative reduction women: 37.2%; men: 28.8%).[26]

From the multicentre CAC Consortium study, 66 636 asymptomatic patients with a CT were assessed, utilizing multivariate regression models for the risk of all-cause mortality and cause-specific mortality based on their CAC score. After adjustments, individuals with CAC ≥1000 had a 5.04-, 6.79-, 1.55-, and 2.89-fold risk of CVD, CAD, cancer, and all-cause mortality, respectively, compared to those with CAC score of 0. The CAC ≥1000 group had a 1.71-, 1.84-, 1.36-, and 1.51-fold increased risk of CVD, CAD, cancer, and all-cause mortality in comparison to those with CAC scores of 400–999. These leads to consider more aggressive preventive treatment for patients with CAC score ≥1000.[27]

The MESA Study investigators assessed the value of CAC for guiding aspirin allocation in primary prevention. All participants (*n* = 6470) underwent a baseline CAC score. CVD risk was estimated using the pooled cohort equation (PCE), defining three strata: <5%, 5–20%, and >20%. Based on PCE the number needed to treat at 5 years (NNT5) was greater than or similar to the number needed to harm (NNH5) among the three estimated cardiovascular risk strata. Conversely, CAC ≥100 and CAC ≥400 identified subgroups in which NNT5 was lower than NNH5. This was true both overall (for CAC ≥100, NNT5 = 140 vs. NNH5 = 518) and within all cardiovascular risk strata. Also, CAC = 0 identified subgroups in which the NNT5 was much higher than the NNH5.[28]

Olsen *i sur.* stratificirali su 48 731 bolesnika prema statusu šećerne bolesti i težini CAD-a (bez bolesti, neopstruktivna ili opstruktivna) s pomoću CT koronarografije (CCTA). Prosječnim praćenjem od 3,6 godina pronašli su da su bolesnici sa šećernom bolesti imali višu stopu smrtnosti od bolesnika bez dijabetesa, neovisno o težini CAD-a. Ipak, bolesnici sa šećernom bolesti bez CAD-a imaju nizak rizik od IM-a, sličan bolesnicima bez dijabetesa.[29]

Finck *i sur.* proveli su istraživanje među 1615 bolesnika sa sumnjom na CAD kojima su morfološki analizirani ateromatozni plakovi primjenom CT koronarografije. Nakon prosječnog vremena praćenja od 10,5 godina bilo je ukupno 36 smrti od kardijalnog uzroka i 15 nefatalnih IM-a. Među obilježjima plaka; uzorak mrljastih ili grubih kalcifikacija i *napkin ring sign* (NRS, središnji dio sa slabim nakupljanjem, a prstenasti dio s višim nakupljanjem) bilo je prediktivno za buduće događaje. Ipak samo uočeni kalcificirani plakovi i NRS nose daljnju dijagnostičku vrijednost povrh kliničkih obilježja i težine koronarne stenoze. U stupnjevitome pristupu predikcija ishoda povrh kliničkog rizika trebala bi biti poboljšana uključenjem težine CAD-a (X^2 od 27,5; P <0,001) uz daljnje diskriminatore za točkaste kalcificirane plakove (X^2 od 3,89; P = 0,049).[30]

Još jedno istraživanje procjenjivalo je mogu li nekalcificirani plakovi s niskom atenuacijom na CCTA imati bolju prediktivnu vrijednost za nastanak IM-a nego vrijednost CAC-a ili procjena težine koronarne stenoze. Pratili su 1769 bolesnika sa sumnjom na anginu pektoris, prosječno 4,7 godina, te su pronašli da je niska atenuacija plaka najjači prediktor IM (P = 0,014), neovisno o zbroju na ljestvici CV rizika, vrijednosti CAC-a ili stenozi koronarnih arterija. Bolesnici s niskom atenuacijom plaka, >4 %, imali su gotovo pet puta veću šansu da se u njih razvije IM (P<0,001).[31]

U istraživanju *PARADIGM* analizirana su 2252 bolesnika koji su bili podvrgnuti klinički indiciranoj CCTA u intervalu od ≥2 godine s neopstruktivnim plakovima (<50 %) u bazičnoj vrijednosti. Cilj studije bio je dokazati jesu li volumen ateroma plaka (PAV), postotak dijametra stenoze (% DS) ili visokorizični plakovi (HRPs) rizičniji za progresiju u opstruktivne lezije (>50 %). Multivarijatnom analizom neovisni pretkazatelji za razvoj opstruktivnih lezija utvrđeni su samo temeljna vrijednost ukupnog PAV-a i % DS (P<0,05), dok za prisutnost HRP-a to nije potvrđeno (P>0.05).[32]

Istraživanje *ICONIC* bilo je usporedna studija bolesnika koji su bili podvrgnuti CCTA prije razvoja akutnoga koronarnog sindroma. Ciljna lezija potvrđena je invazivnom koronarnom angiografijom te je provedena usporedba s bazičnim slikama na CCTA. Pronašli su da HRPs na bazičnom CCTA manje prisutni u neopstruktivnih plakova (19,7 %) nego kod opstruktivnih plakova (46,8 %). Osim toga, neopstruktivni plakovi činili su 81,3 % svih HRPs. Među bolesnicima s identificiranim pretečama ciljne lezije prilagođeni omjer rizika bio je 1,85 (95 % CI 1,26 – 2,72) za HRP, bez interakcije između % DS-a i HRP-a. U usporedbi s neopstruktivnim HRP lezijama, opstruktivne lezije bez obilježja HRP-a pokazale su nesignifikantan omjer rizika od 1,41 (95% CI 0,61 – 3,25) (**slika 2**).[33]

Nedavno su prikazani jednogodišnji rezultati iz Registra *ADVANCE* u 4288 bolesnika sa sumnjom na CAD, u kojih je CCTA utvrdila 30 %-tnu koronarnu stenozu. Evaluirali su frakcijsku rezervu protoka izvedenu CCTA (FFR_{CT}) s kliničkim ishodima. Bilo je 55 događaja, a 78 % njih pojavilo se u bolesnika s vrijednostima FFR_{CT}-a ≤0,80 (P = 0,06). Vrijeme do prvog do-

Olesen *et al.* stratified 48 731 patients by diabetes status and CAD severity (no, non-obstructive, or obstructive) assessed by coronary CT angiography (CCTA). With the median follow-up of 3.6 years, they found that diabetic patients had higher death rates than non-diabetic patients, irrespective of CAD severity. Still, those diabetic patients without CAD have a low risk of MI similar to non-diabetic patients.[29]

Finck *et al.* conducted a study with 1615 patients with suspected CAD who underwent a CCTA with morphological analysis of the atheromatous plaque. After an average of 10.5 years, there were 36 cardiac deaths and 15 non-fatal MI. Among characteristics of the plaque; the spotty or gross calcification pattern and the napkin ring sign (NRS) (low-attenuating central portion with ring-like higher attenuation) were predictive for events. Yet, only spotted calcified plaques and NRS convey further prognostic value above clinical features and the severity of coronary stenosis. In a stepwise approach, the prediction of endpoint beyond clinical risk could be improved by including the severity of CAD (x^2 of 27.5, $P < 0.001$) and further discrimination for spotty calcified plaques (x^2 of 3.89, $P = 0.049$).[30]

Another study assessed whether non-calcified low-attenuation plaque burden on CCTA might have a better predictor of MI than CAC or coronary stenosis severity. They followed up 1769 patients with suspected angina for median 4.7 years finding that low-attenuation plaque burden was the strongest predictor of MI ($P = 0.014$), irrespective of cardiovascular risk score, CAC score, or coronary artery stenosis. Patients with low-attenuation plaque burden >4% were almost five times more likely to have subsequent MI ($P < 0.001$).[31]

From the PARADIGM Study, 2252 patients who underwent clinically indicated serial CCTA at an interscan interval of ≥2 years with non-obstructive plaques (<50%) at baseline were studied. The aim was to prove whether the plaque atheroma volume (PAV), the percentage of diameter stenosis (%DS) or high-risk plaques (HRPs) were more likely to progress to obstructive lesions (>50%). On multivariate analysis, only the baseline total PAV and %DS independently predicted the development of obstructive lesions ($P < 0.05$), whereas the presence of HRP did not ($P > 0.05$).[32]

The investigators of the ICONIC study performed a nested case–control study of patients who underwent a CCTA prior developing an acute coronary syndrome. Culprit lesions were confirmed by invasive coronary angiography and coregistered to baseline CCTA images. They found that HRPs on baseline CCTA were less prevalent in non-obstructive plaques (19.7%) than in obstructive plaques (46.8%). Even though non-obstructive plaque comprised 81.3% of HRP lesions overall. Among patients with identifiable culprit lesion precursors, the adjusted HR was 1.85 (95% CI 1.26–2.72) for HRP, with no interaction between %DS and HRP. Compared to non-obstructive HRP lesions, obstructive lesions without HRP exhibited a non-significant HR of 1.41 (95% CI 0.61–3.25) (**Figure 2**).[33]

Recently, the ADVANCE Registry presented its 1-year results of 4288 patients with suspected CAD in whom a 30% coronary stenosis was identified by CCTA. They evaluated the relationship of fractional flow reserve derived from CCTA (FFR_{CT}) with clinical outcomes. There were 55 events; 78% of them occurred in patients with an FFR_{CT} ≤0.80 ($P = 0.06$). Time to first event (cardiovascular death or MI) occurred more in patients with an FFR_{CT} ≤0.80 compared with FFR_{CT} >0.80 patients (25 [0.80%]

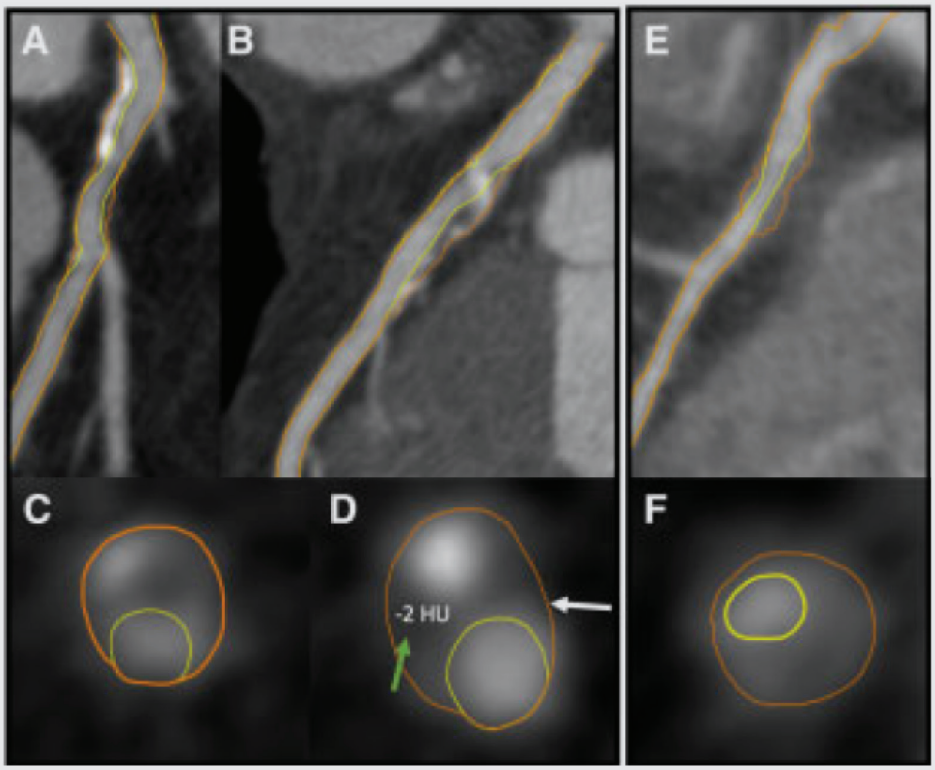

FIGURE 2. Coronary computed tomography angiograms demonstrating high-risk plaque (HRP) in culprit lesion precursors. A 61-year-old male exsmoker exhibited a high-risk plaque extending from the (A) left main to the (B) proximal left anterior descending artery with (C) 41% diameter stenosis severity, (D) positive remodelling (white arrow), and low-attenuation plaque (green arrow). There is also diffuse calcification. One month later, the patient presented with a non-ST-elevation myocardial infarction. A 55-year-old male with hypertension and hyperlipidaemia exhibited a high-risk plaque with (E) only 35% DS severity, but (F) positive remodelling, low-attenuation plaque, and napkin-ring sign. The patient presented with a non- ST-elevation myocardial infarction 2months later. Reproduced with permission from Ferraro et al.[33]

(from Zamorano JL, Pinto FJ, Solano-López J, Bucciarelli-Ducci C. The year in cardiovascular medicine 2020: imaging. Eur Heart J. 2021 Feb 14;42(7):740-749. https://doi.org/10.1093/eurheartj/ehaa1035, by permission of OUP on behalf of the ESC)

gađaja (CV smrt ili IM) pojavilo se u više bolesnika s FFRCT ≤0,80 u usporedbi s bolesnicima s vrijednostima FFRCT-a >0,80 (25[0,80%] prema 3 [0,20%]; relativni rizik (RR):4,22; 95% CI 1,28 – 13,95; P = 0,001). Većina bolesnika u kojih je preporučena strategija liječenja medikamentnom terapijom na osnovi FFRCT-a nastavilo je samo medikamentnu terapiju godinu dana (92,9 %), a, ako je preporuka bila revaskularizacija, većina je (68,9%) bila revaskularizirana.[34]

Inovativna studija predlaže novi parametar dinamičke CT perfuzije (CTP) nazvan *stress MBF rate* (SFR). Ovo je definirano kao omjer hiperemijske (ATP infuzije) MBF u arteriji sa stenozom prema hiperemijskoj MBF u zdravoj arteriji. Osamdeset dva bolesnika upućena su na invazivnu angiografiju zbog sumnje na CAD. Stres dinamički CTP i CCTA izvedeni su prije invazivne koronarografije. Od 101 žila s 30 – 90 %-tnim stenozama na invazivnoj koronarografiji, FFR je rezultirao hemodinamski značajnim promjenama (<0,80) u 47,5 % njih. SFR je bio niži za invazivno detektirane FFR <0,80 lezije (0,66 prema 0,90; P<0,01). U usporedbi s ≥50 %-tnim stenozama CTA, specifičnost za detekciju ishemije SFR-om porasla je s 43 % na 91 %, dok se senzitivnost smanjila s 95 % na 62 %. Kombi-

vs. 3 [0.20%]; relative risk (RR): 4.22; 95% CI: 1.28–13.95; *P* = 0.01). Concerning the downstream care, the majority of patients in whom medical therapy was the recommended treatment strategy following FFR_{CT} continued on only medical therapy at 1 year (92.9%), and when the site recommendation was for revascularization, the majority (68.9%) were revascularized.[34]

An innovative study introduces a new parameter of dynamic CT perfusion (CTP) called stress MBF rate (SFR). This is defined as the ratio of hyperaemic (ATP infusion) MBF in an artery with stenosis to the hyperaemic MBF in a non-diseased artery. Eighty-two patients were derived to invasive angiography for suspected CAD. Stress dynamic CTP and CCTA was performed before invasive angiography. Out of 101 vessels with 30–90% stenosis on invasive angiography, FFR resulted hemodynamically significant (<0.80) in 47.5% of them. SFR was lower for invasive FFR < 0.80 lesions (0.66 vs. 0.90; *P* < 0.01). Compared with ≥50% stenosis by computed tomography angiography (CTA), the specificity for detecting ischaemia by SFR increased from 43% to 91%, whilst the sensitivity decreased from 95% to 62%. The combination of steno-

nacija stenoza ≥50 % s CTA i SFR rezultirala je AUC 0,91, što je mnogo više u usporedbi sa samo MBF-om.[35]

Nuklearno oslikavanje

Još uvijek je predmet rasprave potencijal dobrobiti ishemijom vođene rane koronarne revaskularizacije u bolesnika s CAD-om na preživljenje.

Petel *i sur.* proveli su istraživanje u jednom centru u 16 029 bolesnika sa sumnjom ili poznatom CAD (srednje dobi 68,6 ± 11,9 godina) koji su bili podvrgnuti miokardnom perfuzijskom oslikavanju (MPI) pomoću rubidium-82 (Rb82) pozitronske emisijske tomografije (PET) u mirovanju i opterećenju. Bili su isključeni oni s vrijednošću LVEF-a <40 %. Nakon srednjeg razdoblja praćenja od 3,7 godina 1277 bolesnika bilo je podvrgnuti ranoj revaskularizaciji (87 % PCI, 13 % CABG), a njih 2493 (15,6 %) su umrla. Nakon prilagodbe, Coxov model pronašao je interakciju između postotka ishemije i rane revaskularizacije (P <0,001 i za ukupnu i za kardijalnu smrtnost). Također je utvrđena dobrobit medikamentne terapije na preživljenje kod 5 %-tne ishemije. Prag ishemije za dobrobit preživljenja niži je od prethodno prijavljenih CT (SPECT) MPI.[36]

U III. fazi prospektivne multicentrične kliničke studije, novi PET MPI obilježivač Fluorine-18 flurpiridaz analiziran je u svojoj dijagnostičkoj učinkovitosti za detekciju značajne CAD (>50 % stenoze na kvantitativnoj ICA) u usporedbi sa SPECT-om. Uključeno je 755 bolesnika (srednje dobi 62,3 ± 9,5 godina). Pokazalo se da PET MPI s novim obilježivačem ima superiorniju senzitivnost s obzirom na SPECT [71,9 %; 95 % CI 67,0 – 76,3 %; P <0,001 u odnosu prema 53,7 % (95% CI 48,5 – 58,8 %)]. Također je superiorniji s obzirom na SPECT za detekciju veličine (P <0,001), kvalitetu slike (P <0,001), dijagnostičku sigurnost (P <0,001) te izloženost radijaciji (6,1 ± 0,4 u odnosu prema 13,4 ± 3,2 mSv; P<0,001). Riječ je o novom dijagnostičkom alatu koji ima bolje mogućnosti dijagnosticiranja kada se uspoređuje se SPECT-om, posebice u populaciji žena, populaciji s pretjeranom tjelesnom težinom te u bolesnika upućenih na farmakološki test opterećenja.[37,38]

Kwiecinski *i sur.* objavili su *post hoc* analizu 293 bolesnika s CAD-om koji su bili podvrgnuti 18-F-NaF PET. U 203 (69 %) bolesnika uočena je povećana koronarna aktivnost [predočen kroz povećanu aktivnost koronarnih mikrokalcifikata (CME)]. Nakon 42 mjeseca prosječnog praćenja, 20 bolesnika (7 %) doživjelo je smrtonosni ili nesmrtonosni IM. Svi su se oni ranije prikazali povećanom koronarnom aktivnosti 18F-NaF. ROC analizom pojavnost IM-a bila je bolje potvrđena primjenom 18 F-NaF CME ljestvice u usporedbi s CAC-om i drugim kliničkim ljestvicama rizika, što je snažan i siguran alat za prepoznavanje koronarnog aterosklerotskog procesa.[39]

Unapređenje mogućnosti u predviđanju neželjenih događaja kroz slikovne metode predstavili su Miller *i sur.* u multicentričnoj studiji usporedbom SPECT-MPI ishemije i visokorizične neperfuzijske SPECT-MPI, te pojavnosti neželjenih kardiovaskularnih događaja. Ukupno je analizirano 16 578 pacijenata s poznatom ili mogućom CAD. Prolazna ishemijska dilatacija (TDI) i poststresne promjene u gibanju stijenke (WMA) bile su neperfuzijski markeri ishemije. Nakon prosječno 4,7 godina praćenja 1842 bolesnika imala su jedan događaj. Autori su uočili veću vjerojatnost pojave MACE-a u bolesnika s blagom ishemijom (<10 %) i TID-om u usporedbi s onima bez TID-a u univarijatnoj analizi (adjusted HR 1,42; P = 0,023). Sličsis ≥50% by CTA and SFR resulted in an AUC of 0.91, which was significantly higher than MBF alone.[35]

Nuclear imaging

Nowadays, the potential survival benefit of ischaemia-guided early coronary revascularization in patients with stable coronary artery disease (CAD) is still in debate.

Patel *et al.* performed a single-centre cohort study including 16 029 patients with suspected or known CAD (mean age 68.6 ± 11.9 years) who underwent a Rubidium-82 (Rb82) rest-stress positron emission tomography (PET) myocardial perfusion imaging (MPI), excluding those with LVEF < 40%. After a median follow-up of 3.7 years, 1277 patients underwent early revascularization (87% PCI, 13% CABG), and 2493 (15.6%) died. After a propensity score adjustment for potential confounders, a Cox model found an interaction between %ischaemia and early revascularization ($P < 0.001$ for both all-cause and cardiac death). They also report medical therapy survival equipoise at 5% ischaemia. This ischaemia threshold for survival benefit is lower than previously reported with single photon emission CT (SPECT) MPI.[36]

In a phase-III prospective multicentric clinical study, the novel PET MPI tracer Fluorine-18 flurpiridaz is evaluated for its diagnostic efficacy detecting significant CAD (>50% stenosis in quantitative ICA) vs. SPECT. 755 patients (mean age 62.3 ± 9.5 years) were included. The PET MPI with the novel tracer demonstrated to have superior sensitivity than SPECT [71.9%, 95% CI 67.0–76.3%; $P < 0.001$ vs. 53.7% (95% CI: 48.5–58.8%)]. It was also superior to SPECT for defect size ($P < 0.001$), image quality ($P < 0.001$), diagnostic certainty ($P < 0.001$), and radiation exposure (6.1 ± 0.4 vs. 13.4 ± 3.2 mSv; $P < 0.001$). This is a new diagnostic tool with better diagnostic performance comparing to SPECT, in particular for women, obese, and patients undergoing pharmacological stress testing.[37,38]

Kwiecinski *et al.* presented a *post hoc* analysis of 293 patients with previous CAD who underwent 18-F-NaF PET. Of those, 203 (69%) showed increased coronary activity [represented by quantitative coronary microcalcification activity (CME)]. After a median follow-up of 42 months, 20 patients (7%) experienced fatal or non-fatal MI. All of them presented previously increased coronary 18F-NaF activity. On an ROC analysis, MI prediction was better for 18F-NaF CME score than coronary calcium scoring and different clinical risk scores. This represents a powerful and safe tool for the detection of coronary atherosclerotic inflammation.[39]

Another proof of improvements of imaging's ability to predict events is the international multicentre study by Miller *et al.* in which they sought to determine the interactions between SPECT-MPI ischaemia, high-risk non-perfusion SPECT-MPI findings and MACE. In total, 16 578 patients with known or suspected CAD were analysed. Transient ischaemic dilation (TID) and post-stress wall motion abnormalities (WMA) were non-perfusion markers of ischaemia. After a median follow-up of 4.7 years, 1842 individuals presented one event. In a univariate analysis, the authors found that patients with mild ischaemia (<10%) and TID were more likely to present MACE compared with patients without TID (adjusted HR 1.42, $P = 0.023$). There were similar findings in patients with post-stress WMA. However, multivariable analysis of patients

ni su dokazi proizašli i kod onih s učinjenim poststresnim WMA. U multivarijatnoj analiza blaga ishemija i TID (prilagođeni omjer šansi 1,50, P = 0,037), no ne i WMA, dovode do povećanja rizika od MACE-a.[40]

Omjer srce/medijastinum (H/M) mjeren kardijalnom scintigrafijom 123I-metajodobenzilgvanidinom (123I-mIBG) ima prognostičku vrijednost u dijagnozi kroničnog zatajivanja srca. Istraživači iz *OPAR Registry* objavili su opservacijsku kohortnu studiju u jednom centru s 349 bolesnika primljenih zbog akutnoga dekompenziranog srčanog zatajivanja. 123I-MIBG scintigrafija i ultrazvuk srca učinjeni su prije otpusta. Od ukupnog broja bolesnika u studiji 127 se prikazalo s reduciranom EF, 78 s HFmrEF i 144 s očuvanom EF. Nakon prosječnog razdoblja praćenja od 2,1 (±1,4) godine, 128 bolesnika se prikazalo ponovnim događajem (hospitalizacija zbog HF-a ili CV smrt). Multivarijabilna Coxova analiza pokazuje da je kasna vrijednost H/M (nakon 200 minuta od primjene tracera) značajno povezan s kardijalnim događajem u čitavoj kohorti (P = 0,0038), kao i u svakoj subgrupi pojedinačno (P = 0,0235 u reduciranoj, P = 0,0119 u *mid-range* i P = 0,0311 u očuvanoj sistoličkoj funkciji). Autori su zaključili kako H/M omjer upućuje na disfunkciju kardijalnoga simpatičkog živčanog sustava, što je povezano s kardijalnim događajima u bolesnika s akutnim srčanim zatajivanjem neovisno o EF-u.[41]

Trećina bolesnika s kroničnim srčanim zatajivanjem koji su predviđeni za ugradnju CRT uređaja prema postojećim preporukama, ne osjeća smanjenje simptoma. Verschure *i sur.* prikazali su rezultate u 78 bolesnika sa stabilnim srčanim zatajivanjem, te kriterijima za ugradnju CRT uređaja kojima su prethodno učinili 123I- MIBG scintigrafiju. Kasni H/M omjer neovisni je prediktor za poboljšanje vrijednosti EF na >35 % (P = 0,0014), a rani H/M omjer za poboljšanje LVEF-a za najmanje 10 % od početne.[42]

Kardijalna amiloidoza (CA) podrazumijeva lošu prognozu za bolesnike. Rano postavljanje dijagnoze s dovoljnom točnošću i sigurnošću i dalje je vrlo zahtjevno. Rosengren *i sur.* objavili su najveću studiju bolesnika s CA (AL i ATTR) dokazani Pittsburškim spojem B (11C-PIB) PET-om. U toj studiji dijagnostička je točnost 11C-PIB PET-a velika uz senzitivnost (94 %) i specifičnost (93 % – 100 %) za razlikovanje CA od neamiloidne hipertrofije i zdrave kontrolne skupine. 11C-PIB apsorpcija signifikantno je veća kod AL-CA nego u bolesnika s ATTR-CA (P < 0,001). Lee *i sur.* također su upozorili na poveznicu između 11C-PIB apsorpcije i miokardne histologije kod CA. Dodatno, nakon prosječnog praćenja bolesnika od 423 dana, stupanj miokardne apsorpcije 11C-PIB-a bio je signifikantni prediktor kliničkog ishoda (smrt, transplantacija srca i akutna srčana dekompenzacija) prema multivarijabilnoj Coxovoj regresijskoj analizi (prilagođen HR 1,185; 95 % CI 1,054 – 1,332; P = 0,005).[43]

Roque *i sur.* koristili su se serijskim snimanjem 18F-fluorodeoxyglucose (FDG) PET/CT nakon 1, 6 i 12 mjeseci u 37 bolesnika nakon zamjene aortalnog ili mitralnog zalistka. Dobili su standardizirane vrijednosti apsorpcije (SUVs) i novu predloženu vrijednost indeksa apsorpcije zalistka [(SUVmax - SUVmean)/SUVmax]. Od učinjenih 111 PET/CT, apsorpcija FDG-a uočena je u 79,3 % bolesnika, koji se prikazuju difuznim homogenim obrascem distribucije u 93 %. Nijedan bolesnik tijekom praćenja nije imao endokarditis (**slika 3**). Iznenađujuće, nije pronađena signifikantna razlika u FDG distribuciji ili apsorpciji vrijednosti između 1, 6 i 12 mjeseci, dovodeći u pitanje tromjesečno postkirurško razdoblje procjene infekcije umjetnog zalistka.[44]

with mild ischaemia, TID (adjusted HR 1.50, *P = 0.*037), but not WMA, was independently associated with increased MACE.[40]

Heart to mediastinum (H/M) ratio measured by cardiac 123I-metaiodobenzylguanidine (123I-mIBG) scintigraphy has demonstrated prognostic significance in the setting of chronic HF. The OPAR Registry investigators describe a single-centre observational cohort study with 349 patients admitted for acute decompensated HF. 123I-MIBG imaging and echocardiography were performed before discharge. Of those 127 presented reduced EF, 78 mid-range EF, and 144 preserved EF. After a median follow-up period of 2.1 (±1.4) years, 128 patients presented cardiac events (HF hospitalization or cardiac death). A multivariable Cox analysis demonstrates that late H/M (after 200 min of tracer) was significantly associated with cardiac events in overall cohort (*P* = 0.0038), as in each EF subgroup (*P* = 0.0235 in reduced, *P* = 0.0119 in mid-range and *P* = 0.0311 in preserved). The authors conclude that H/M ratio reflects cardiac sympathetic nerve dysfunction, which is associated with cardiac events in acute HF patients, irrespective of EF.[41]

One-third of chronic HF patients who assign to CRT therapy based on guidelines classical eligibility criteria does not present benefits. Verschure *et al.* presented their results in 78 stable HF individuals with guideline-based criteria for CRT who underwent a cardiac 123I-mIBG imaging before device implantation. Late H/M ratio was an independent predictor of LVEF improvement to >35% (*P* = 0.0014) and early H/M for LVEF improvement of at least 10% from basal.[42]

CA implies ominous prognosis for patients. Early diagnosis with sufficient accuracy and safety remain still challenging. Rosengren *et al.* published the largest study of CA patients (both AL and ATTR) examined with Pittsburgh compound (11C-PIB) PET. In this study, the diagnostic accuracy of 11C-PIB PET is remarkable with high sensitivity (94%) and specificity (93% to 100%) for distinguishing CA patients from both non-amyloid hypertrophic and healthy controls. 11C-PIB uptake was significantly higher in AL-CA patients than in ATTR-CA patients (*P* < 0.001). In the study from Lee *et al.*, they also demonstrate correlation between 11C-PIB uptake and myocardial histology in CA. In addition, after a median follow-up of 423 days, the degree of myocardial 11C-PIB uptake was a significant predictor of clinical outcome (death, heart transplantation, and acute decompensated HF) on multivariate Cox regression analysis (adjusted HR: 1.185; 95% CI 1.054–1.332; *P* = 0.005).[43]

Roque *et al.* used serial 18F-fluorodeoxyglucose (FDG PET/CT) after 1, 6, and 12 months in 37 post-aortic or mitral valve replacement patients. They obtained the standardized uptake values (SUVs) and a new proposed value denominate valve uptake index [(SUVmax – SUVmean)/SUVmax]. Of the 111 PET/CT performed, FDG uptake was visually detectable in 79.3% of patients, presenting a diffuse, homogeneous distribution pattern in 93%. No patient presented endocarditis during follow-up (**Figure 3**). Surprisingly, no significant differences were encountered in FDG distribution or uptake values between 1, 6, or 12 months, questioning the 3-month post-surgical period for the assessment of prosthetic infection.[44]

Tam *et al.* presented a study of FDG PET/CT in suspected LV assist devices (LVAD) associating their single-centre retrospective cases between September 2015 and February 2018 with a systematic review of PubMed from database inception through March 2018 involving in total 119 scans. Pooled sensi-

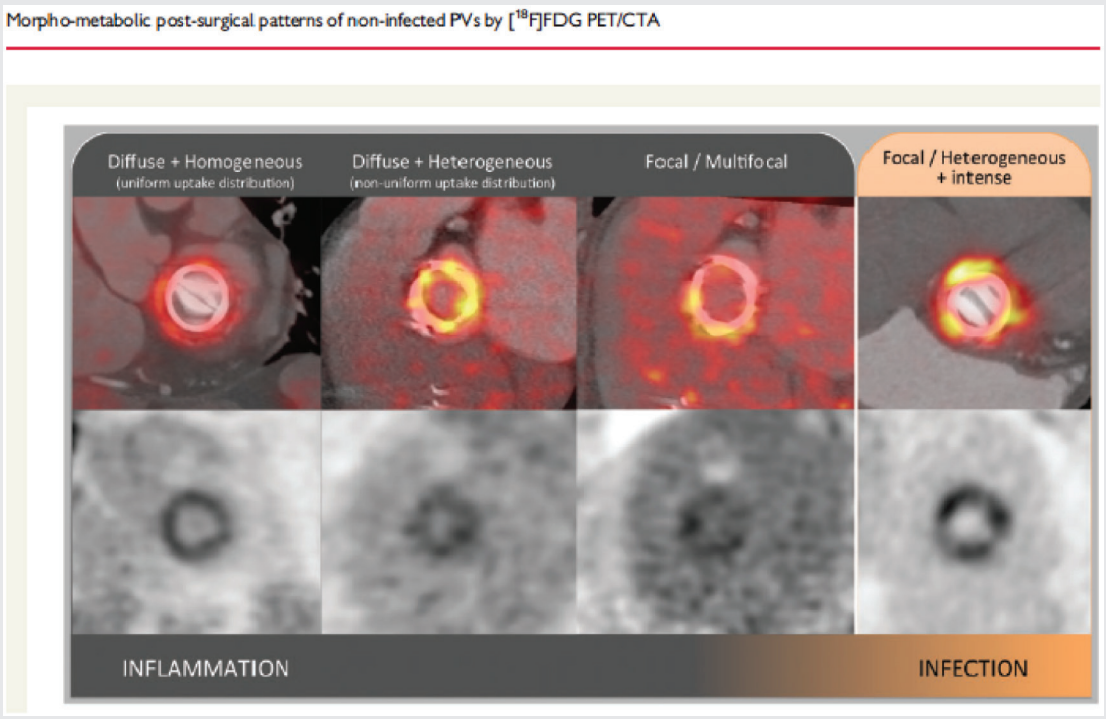

FIGURE 3. 18F-fluorodeoxyglucose uptake distribution patterns (visual assessment). 18F-fluorodeoxyglucose uptake in non-infected prostheses (left panel), compared with an example of prosthetic valve endocarditis (right panel). Positron emission tomography/CTA fusion images of the valve plane (upper row), and their corresponding attenuation-corrected positron emission tomography images (lower row). From left to right, the characteristic inflammation patterns in order of descending frequency: diffuse homogeneous (93%), diffuse heterogeneous (7%), and focal/multifocal (2%). The diffuse homogeneous pattern is characteristic of inflammation and clearly differentiable from infection, whereas more focal. 18F-fluorodeoxyglucose uptake may overlap with infective endocarditis. No anatomic lesions were detected in any patient. Reproduced with permission from Roque et al.[44]

(from Zamorano JL, Pinto FJ, Solano-López J, Bucciarelli-Ducci C. The year in cardiovascular medicine 2020: imaging. Eur Heart J. 2021 Feb 14;42(7):740-749. https://doi.org/10.1093/eurheartj/ehaa1035, by permission of OUP on behalf of the ESC)

Tam *i sur.* prikazali su istraživanje FDG PET/CT-a pri sumnji na infekciju uređaja za potpomognutu funkciju lijeve klijetke (LVAD). Povezali su retrospektivne slučajeve jednog centra u razdoblju od rujna 2015. do veljače 2018. sa sistematskim pregledom literature iz baze podataka *PubMed* u ožujku 2018., uključujući ukupno 119 prikaza. Ukupna je osjetljivost je bila 92 % (95 % CI: 82 % – 97 %) i specifičnost 83 % (95 % CI: 24 % – 99 %) za FDG PET/CT u dijagnosticiranju infekcija LVAD sustava. ROC analiza pokazala je AUC od 0,94 (95 % CI 0,91 – 0,95).[45]

Još jedan scenarij dokaza infekcije u kojem oslikavanje nuklearnim tehnikama ima važnu ulogu jest endokarditis povezan s implantacijom srčanih uređaja (CDRIE). Holcman *i sur.* procijenili su dijagnostičku točnost hibridne SPECT CT tehnike s pomoću tehnecijum 99meta heksametilpropilenamino oksimom označenih leukocita (99mTc-HMPAO-SPECT/CT). U prospektivno istraživanje u jednom centru uključena su 103 bolesnika sa suspektnim CDRIE u kojih je proveden 99mTc-HMPAO-SPECT/CT. Ustanovili su da dodatak ove tehnike nuklearnog oslikavanja poboljšava senzitivnost modificiranih Dukeovih kriterija (87 % prema 48 %, P< 0,001) i gdje negativan prikaz s viskom vjerojatnošću isključuje CDRIE. Ovo dovodi do redukcije u mogućoj dijagnozi CDRIE-a.[46]

tivity was 92% (95% CI: 82%–97%) and specificity was 83% (95% CI: 24%–99%) for FDG PET/CT in diagnosing LVAD infections. The ROC curve analysis demonstrated an AUC of 0.94 (95% CI 0.91–0.95).[45]

Another infectious scenario in which nuclear imaging techniques play an important diagnostic role is cardiac device-related infected endocarditis (CDRIE). Holcman *et al.* assessed the diagnostic accuracy of the hybrid technique of SPECT CT with technetium99mhexamethylpropyleneamine oxime-labelled leucocytes (99mTc-HMPAO-SPECT/CT). In a single-centre prospective study, 103 patients with suspected CDRIE who underwent 99mTc-HMPAO-SPECT/CT were included. They found that adding this nuclear technique improves the sensitivity of the modified Duke criteria alone (87% vs. 48%, $P < 0.001$), whereas a negative scan excludes CDRIE with high probability. This yielded a reduction in possible CDRIE diagnoses.[46]

Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

Conflict of interest: none declared.

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