Godina 2017. u kardiologiji: oslikavanje

The year in cardiology 2017: imaging

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Preambula

Ovaj pregledni članak donosi novosti objavljene u vezi s neinvazivnim kardiovaskularnim oslikavanjem. Iako je ehokardiografija dobro poznata kao metoda prvog izbora u evaluaciji bolesnika sa simptomima kardiovaskularnih bolesti, i druge su tehnike (tehnike nuklearne medicine, magnetna rezonancija srca i kompjutorizirana tomografija) potrebne za oslikavanje specifičnih obilježja bolesti ili patofizioloških mehanizama koji mogu utjecati na liječenje bolesnika. Dokazi koji upućuju na rastuću dijagnostičku i prognostičku vrijednost kombinacija slikovnih metoda ili fuzijskih slikovnih tehnika eksponencijalno rastu. Napredak u neinvazivnim tehnikama oslikavanja dao je važne nove uvide u patofiziologiju valvularnih bolesti srca i kardiomiopatija, stratifikacije rizika u bolesnika sa sumnjom na koronarnu bolest srca te dijagnostiku komplikacija vezanih za implantabilne uređaje ili biološke proteze. Ovaj članak pruža pregled najrelevantnijih članaka objavljenih u 2017. godini.

Preamble

This Year in Cardiology 2017 review article provides a broad overview of the novelties published in non-invasive cardiovascular imaging. While it is well established that echocardiography is the imaging technique of first choice to evaluate patients with cardiovascular symptoms, other techniques (nuclear imaging, cardiovascular magnetic resonance, and computed tomography) are needed to image specific-disease characteristics or pathophysiological mechanisms that may impact on the patient's management. The evidence showing the incremental diagnostic and prognostic value of combination of imaging techniques or fusion imaging is growing exponentially. Advances in non-invasive cardiac imaging have provided important new insights in the pathophysiology of valvular heart disease and cardiomyopathies, risk stratification of patients with suspected coronary artery disease and diagnosis of implanted device- or bioprosthesis-related complications; this article provides an overview of the most relevant articles published in 2017.

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Uvod

Napredak u neinvazivnim tehnikama oslikavanja dao je važne nove uvide u patofiziologiju valvularnih bolesti srca i kardiomiopatija, stratifikacije rizika u bolesnika sa sumnjom na koronarnu bolest srca (CAD) te dijagnostiku komplikacija vezanih za implantabilne uređaje ili biološke proteze. Dokazi koji upućuju na rastuću dijagnostičku i prognostičku vrijednost kombinacija slikovnih metoda ili fuzijskih slikovnih tehnika eksponencijalno rastu. Ovaj članak donosi pregled novosti objavljenih na području neinvazivnog kardiovaskularnog oslikavanja u 2017. godini.

Ehokardiografija

Uloga ehokardiografije u dijagnostici bolesti srčanih zalistaka naglašena je u *OxValve* populacijskoj kohortnoj studiji koja je uključila 2500 bolesnika u dobi od 65 i više godina bez poznatih bolesti zalistaka.[1] Jedan od dvojice pacijenata u ovome uzorku imao je novodijagnosticiranu (uglavnom blagu) bolest srčanih zalistaka: 34 % aortnu sklerozu, 22 % mitralnu regurgitaciju i 15 % aortalnu regurgitaciju. Srednje teška i teška nedijagnosticirana bolest srčanih zalistaka registrirana je u 6,4 % bolesnika. Zanimljivo, srednje teška i teška valvularna bolest bila je triput češća u bolesnika s fibrilacijom atrija (AF), što bi se moglo smatrati znakom značajne nijeme valvularne bolesti. Projekcije temeljene na populacijskoj kohortnoj studiji *OxValve* nagovješćuju da će broj osoba starijih od 65 i više godina u Ujedinjenom Kraljevstvu porasti s 1,5 milijuna u 2015. na 3 milijuna do 2046. godini. Rezultati ove studije pružaju daljnje uvide u patofiziologiju i prirodni tijek bolesti srčanih zalistaka te imaju važne implikacije na liječenje bolesnika u trenutačnoj eri s rastućim napretkom u endovaskularnom liječenju.

Odabir bolesnika koji bi mogli profitirati od valvularnih intervencija oslanja se na simptome te učinke abnormalnih uvjeta punjenja srčanih šupljina. Opseg oštećenja srca uzrokovan abnormalnom valvularnom hemodinamikom važan je čimbenik pobola/smrtnosti u bolesnika s valvularnim bolestima. U studiji PARTNER-2 ukupno je 1661 bolesnik s teškom aortnom stenozom klasificiran u četiri stadija na osnovi oštećenja srca procijenjenog ehokardiografijom: bez oštećenja srca, osim valvularnog (stadij 0, n = 47), oštećenje lijeve klijetke (LV) karakterizirano povećanim indeksom mase LV-a (stadij 1, n = 212), oštećenje lijevog atrija (LA) ili oštećenje mitralne valvule, uključujući proširenje LA-a, srednje tešku i tešku mitralnu regurgitaciju i AF (stadij 2, n = 814), oštećenje plućnih krvnih žila ili trikuspidne valvule karakterizirano sistoličkom plućnom hipertenzijom i srednje teškom ili teškom trikuspidnom regurgitacijom (stadij 3, n = 413) i oštećenje desne klijetke karakterizirano srednje teškom i teškom ventrikularnom disfunkcijom (stadij 4, n = 145).[2] Jednogodišnja smrtnost nakon zamjene aortne valvule rasla je s progresijom oštećenja: od 4,4 % u stadiju 0 do 24,5 % u stadiju 4. Svaki porast u stadiju bio je neovisno povezan s porastom smrtnosti [omjer hazarda (HR) 1,46, 95 %-tni interval pouzdanosti (CI) 1,27 – 1,67; P < 0,0001].

Bolesnici sa simptomatskom aortnom stenozom niskog protoka / niskog gradijenta mogu imati znatno oštećenje srca s koncentričnom hipertrofijom LV-a i restriktivnom fiziologijom, slično amiloidozi srca. Od 6 % do 12 % takvih bolesnika može imati transtiretinsku amiloidozu srca.[3,4] U 151 bolesni-

Introduction

Advances in non-invasive cardiac imaging have provided important new insights in the pathophysiology of valvular heart disease and cardiomyopathies, risk stratification of patients with suspected coronary artery disease (CAD), and diagnosis of implanted device- or bioprosthesis-related complications. The evidence showing the incremental diagnostic and prognostic value of combination of imaging techniques or fusion imaging is growing rapidly. This Year in Cardiology 2017 review article provides a broad overview of the novelties published in non-invasive cardiovascular imaging.

Echocardiography

The role of echocardiography in the diagnosis of valvular heart disease was underscored in the OxValve Population Cohort Study which recruited 2500 patients aged 65 years and older without known valvular heart disease.[1] One in two of the elderly population had newly diagnosed (predominantly mild) valvular heart disease: 34% presented aortic sclerosis, 22% mitral regurgitation, and 15% aortic regurgitation. Moderate and severe undiagnosed valvular heart disease was identified in 6.4% of patients. Interestingly, moderate and severe valvular heart disease was three times more common in patients with atrial fibrillation (AF), which could be considered as a marker of silent significant valvular heart disease. Projections based on the OxValve Population Cohort Study suggest that the number of individuals aged 65 years or more in the UK will increase from 1.5 million in 2015 to 3 million by 2046. The results of this study provide further insights in the pathophysiology and natural history of valvular heart disease and have important implications for the management of elderly patients in the current era with growing advances in transcatheter therapies.

Selection of patients who may benefit from valvular intervention relies on symptoms and effects of the abnormal loading conditions on the cardiac chambers. The extent of cardiac damage caused by the abnormal valve haemodynamics is an important determinant of the morbi-mortality of patients with heart valve disease. From the Placement of Aortic Transcatheter Valves (PARTNER)-2 trials, 1661 patients with severe stenosis were classified into four stages based on the cardiac damage assessed with echocardiography: no extra-valvular cardiac damage (Stage 0, $n = 47$), left ventricular (LV) damage characterized by increased LV mass index (Stage 1, $n = 212$), left atrial (LA), or mitral damage, including LA dilation, moderate, and severe mitral regurgitation and AF (Stage 2, $n = 814$), pulmonary vasculature or tricuspid damage characterized by systolic pulmonary hypertension and moderate or severe tricuspid regurgitation (Stage 3, $n = 413$) and right ventricular damage characterized by moderate and severe right ventricular dysfunction (Stage 4, $n = 145$).[2] One-year mortality rates after aortic valve replacement increased along with progression of cardiac damage stage: from 4.4% in stage 0 to 24.5% in Stage 4. Each increment in cardiac damage stage was independently associated with increased mortality [hazard ratio (HR) 1.46, 95% confidence interval (CI) 1.27–1.67; $n < 0.0001$].

Patients with symptomatic low-flow, low-gradient severe aortic stenosis may display significant cardiac damage with concentric LV hypertrophy and restrictive physiology, resembling cardiac amyloidosis. Between 6% and 12% of such patients may have transthyretin cardiac amyloidosis.[3,4] In 151

ka s teškom aortnom stenozom koji su podvrgnuti transkateterskoj implantaciji aortne valvule učinjena je scintigrafija srca s tehnecij-99m pirofosfatom (^{99m}Tc-PYP) radi evaluacije prisutnosti prateće transtiretinske amiloidoze srca. Također je učinjena tkivna doplerska ehokardiografija, kao i globalni longitudinalni strain (GLS) LV s dvodimenzionalnom *speckle tracking* ehokardiografijom radi procjene sistoličke funkcije LV.[5] Šesnaest posto bolesnika imalo je pozitivan nalaz scintigrafije s ^{99m}Tc-PYP na transtiretinsku amiloidozu srca. U usporedbi s bolesnicima koji su imali izoliranu tešku aortnu stenozu, bolesnici s pratećom transtiretinskom amiloidozom srca imali su izraženiju hipertrofiju LV-a, niži udarni volumen, viši stupanj dijastoličke disfunkcije LV-a te reduciranu funkciju LV-a [nižu ejekcijsku frakciju LV (EF), više oslabljenu LV GLS i nižu vršnu sistoličku brzinu na tkivnoj doplerskoj ehokardiografiji. S'] (**slika 1A – Take-home figure**) Vrijednost S' ≤6 cm/s na tkivnoj doplerskoj ehokardiografiji snažno je povezana s pozitivnim nalazom ^{99m}Tc-PYP scintigrafije. Kliničke implikacije ovih nalaza tek trebaju biti procijenjene u većim studijama koje bi potvrdile da bolesnici s pratećom transtiretinskom amiloidozom srca imaju lošiju prognozu nakon zamjene aortne valvule u usporedbi s bolesnicima s izoliranom aortnom stenozom.

Uloga trodimenzionalne transezofagealne ehokardiografije u boljoj karakterizaciji anatomije mitralne valvule te dinamici mitralne regurgitacije naglašena je u nekoliko radova. Kagiyama *i sur.*[6] dokazali su prisutnost nedostatne pregradnje mitralnih listića procijenjene trodimenzionalnom transezofagealnom ehokardiografijom u 28 bolesnika s AF-om i srednje teškom ili teškom mitralnom regurgitacijom u usporedbi s 56 bolesnika s AF-om bez mitralne regurgitacije. Omjer između ukupne površine listića i površine mitralnog prstena mnogo je manji u bolesnika sa srednje teškom i teškom mitralnom

patients with severe aortic stenosis undergoing transcatheter aortic valve implantation, technetium-99 m pyrophosphate (^{99m}Tc-PYP) cardiac scintigraphy was performed to evaluate the presence of concomitant transthyretin cardiac amyloidosis and tissue Doppler echocardiography, as well as LV global longitudinal strain (GLS) with two-dimensional speckle tracking echocardiography to assess LV systolic function.[5] Sixteen percent of patients had a ^{99m}Tc-PYP scan positive for transthyretin cardiac amyloidosis. Compared to patients with isolated severe aortic stenosis, patients with concomitant transthyretin cardiac amyloidosis showed more LV hypertrophy, lower stroke volume, more advanced LV diastolic dysfunction, and reduced LV function [lower LV ejection fraction (EF), more impaired LV GLS and lower peak systolic velocity on tissue Doppler imaging, S'] (**Figure 1A** – **Take home figure**). A value of S' ≤6 cm/s on tissue Doppler echocardiography was strongly associated with a positive ^{99m}Tc-PYP scan. The clinical implications of these findings need to be evaluated in larger studies confirming that patients with concomitant transthyretin cardiac amyloidosis have worse prognosis after aortic valve replacement as compared to patients with isolated aortic stenosis.

The role of three-dimensional transoesophageal echocardiography to better characterize the mitral valve anatomy and dynamics in mitral regurgitation was highlighted in several publications. For example, Kagiyama *et al.*[6] demonstrated the presence of insufficient remodelling of the mitral leaflets assessed with three-dimensional transoesophageal echocardiography in 28 AF patients with moderate and severe mitral regurgitation compared to 56 AF patients without mitral regurgitation. The ratio between the total leaflet area and the mitral annulus area was significantly smaller among patients with moderate and severe mitral regurgitation than in patients without (1.29 ± 0.10 vs. 1.65 ± 0.24, P < 0.001) indicating insuffi-

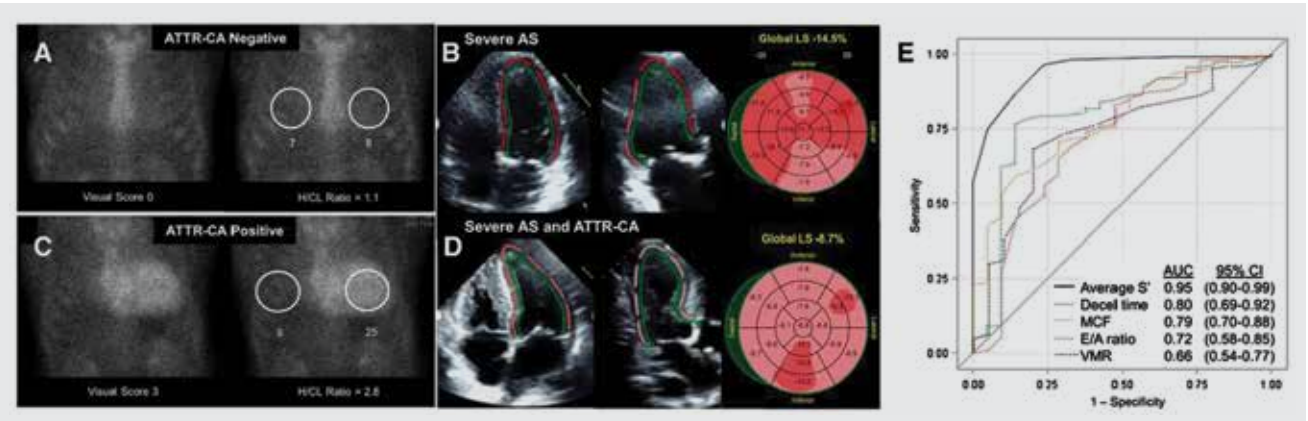

FIGURE 1A. Take home figure. Transthyretin cardiac amyloidosis in patients with severe aortic stenosis. Panels A and B show the technetium-99m pyrophosphate (^{99m}Tc-PYP) cardiac scintigraphy and the left ventricular global longitudinal strain bull's eye plot of a patient without transthyretin cardiac amyloidosis. A ^{99m}Tc-PYP cardiac scintigraphy positive for transthyretin cardiac amyloidosis shows an increased heart-to-contralateral ratio (H/CL) (panel C) and more impaired left ventricular global longitudinal strain (panel D). Panel E shows the receiver operating curves for several echocardiographic parameters of left ventricular systolic and diastolic dysfunction. The S' measured on tissue Doppler imaging had the largest area under the curve to predict ^{99m}Tc-PYP cardiac scintigraphy positive for transthyretin cardiac amyloidosis. Reproduced with permission from Castano *et al.*[3]

AS, aortic stenosis; ATTR-CA, transthyretin cardiac amyloidosis; AUC, area under the curve; CI, confidence interval; Decel, deceleration; H/CL, heart-to-contralateral ratio; LS, longitudinal strain; MCF, myocardial contraction fraction; VMR, voltage-mass ratio.

regurgitacijom nego u bolesnika bez nje (1,29 ± 0,10 prema 1,65 ± 0,24, P < 0,001), što upućuje na nedostatni rast (pregradnju) mitralnih listića da bi kompenzirali dilataciju mitralnog prstena u AF-u (što je rezultiralo znatnom mitralnom regurgitacijom). Nadalje, van Wijngaarden *i sur.*[7] dokazali su različitu dinamiku prstena mitralne valvule na trodimenzionalnoj transezofagealnoj ehokardiografiji u bolesnika s teškom mitralnom regurgitacijom zbog fibroelastičnog nedostatka, Barlowljeve bolesti i sekundarne mitralne regurgitacije. Tijekom srčanog ciklusa mitralni je prsten ostao plosnat i manje dinamičan (omjer visine prstena i širine komisure bio je 18,24 ± 4,9 u ranoj sistoli, 18,24 ± 4,7 u sredini sistole i 17,67 ± 4,4 u kasnoj sistoli, P = 0,083) u bolesnika sa sekundarnom mitralnom regurgitacijom, dok su bolesnici s fibroelastičnim nedostatkom i Barlowljevom bolešću imali naglašenije sedlasti mitralni prsten koji je postao plosnatiji tijekom kasne sistole (omjer visine prstena i širine komisure promijenio se s 21,99 ± 4,83 na 17,39 ± 4,2 u bolesnika s fibroelastičnim nedostatkom, a s 23,89 ± 4,05 na 15,36 ± 4,2 u bolesnika s Barlowljevom bolešću; P < 0,001 za sve). Ovi nalazi upućuju na to da je mehanika mitralnog prstena važna patofiziološka odrednica disfunkcije mitralnog zalistka.

Standardizacija novih ehokardiografskih tehnika ključna je za njihovu implementaciju u rutinsku kliničku praksu. Mjerenje GLS LV-s ima manje varijabilnosti od LVEF-a pri kontrolnim pregledima.[8] Za usporedbu, procjena regionalnoga longitudinalnog naprezanja LV-a pokazala je veću varijabilnost među dobavljačima.[9] Razlike u kvaliteti slike, algoritmima za praćenje i redukciju buke vremenskim i prostornim uglađivanjem preko raznih dobavljača moglo bi objasniti visoku varijabilnost mjerenja regionalnog naprezanja. Reproducibilnost mjerenja GLS LV-a i regionalnog naprezanja važni su kada je potrebna ehokardiografska kontrola. U bolesnika koji su na terapiji zbog karcinoma, rana detekcija disfunkcije srca ključna je radi pravodobne implementacije kardioprotektivnih terapija u prevenciji ireverzibilne kardiotoksičnosti. Mjerenje naprezanja LV-a daje senzitivnije markere sistoličke disfunkcije LV-a nego LVEF, što bi moglo omogućiti raniju detekciju oštećenja srca. U kakvom su ove mjere odnosu s ventrikulsko-arterijskim spojem u ovoj podgrupi bolesnika procjenjivali su Narayan *i sur.*[10] Od 135 bolesnika s karcinomom dojke koji su dobivali doksorubicin i trastuzumab, u 15 % njih razvila se kardiotoksičnost tijekom medijana praćenja od 1,9 godina. Omjer između efektivne elastičnosti i endosistoličke elastičnosti (mjere ventrikulsko-arterijskog spoja) te cirkumferencijske napetosti LV-a pri prvom mjerenju pokazao je najveću površinu ispod krivulje (AUC) u predviđanju za kemoterapiju vezane kardiotoksičnosti (0,703, odnosno 0,655). Međutim, ove AUC pokazuju skromnu diskriminirajuću sposobnost u identificiranju bolesnika u kojih će se razviti kardiotoksičnost. Randomizirane kliničke studije bile bi idealne u utvrđivanju vanjske validnosti ovih nalaza.

Oslikavanja primjenom nuklearnih metoda

Nuklearne metode oslikavanja pružaju jedinstvene dodatne informacije koje proširuju saznanja dobivena drugim slikovnim metodama. No nuklearno oslikavanje uključuje ionizirajuće zračenje. U nedavnom dokumentu koji su objavile tri velike europske profesionalne organizacije na polju kardiovaskularnog oslikavanja, prikazana je najbolja praksa (tehnologija, radioizotopi i prikupljanje podataka) kako postići

cient growth (remodelling) of the mitral leaflets to compensate for the dilation of the mitral annulus in AF (which then resulted in significant mitral regurgitation). Furthermore, van Wijngaarden *et al.*[7] demonstrated the different dynamics of the mitral valve annulus on three-dimensional transoesophageal echocardiography in patients with severe mitral regurgitation due to fibroelastic deficiency, Barlow's disease, and secondary mitral regurgitation. The mitral annulus dimensions were largest in patients with Barlow's disease whereas no differences were observed between patients with fibroelastic deficiency and patients with secondary mitral regurgitation. Along the cardiac cycle, the mitral annulus remained flat and less dynamic (the annulus height to the commissural width ratio was 18.24 ± 4.9 at early systole, 18.24 ± 4.7 at mid-systole, and 17.67 ± 4.4 at late systole, $P = 0.083$) in patients with secondary mitral regurgitation whereas patients with fibroelastic deficiency and Barlow's disease had more pronounced saddle-shaped mitral annulus which became significantly flatter at late systole (the annulus height to commissural width ratio changed from 21.99 ± 4.83 to 17.39 ± 4.2 in fibroelastic deficiency patients and from 23.89 ± 4.05 to 15.36 ± 4.2 in Barlow's disease patients; $P < 0.001$ for all). These findings suggest that mitral annulus mechanics are important pathophysiological determinants of the mitral valve dysfunction.

Standardization of novel echocardiographic techniques is key for implementation in routine clinical practice. Left ventricular GLS measurement has better inter-observer agreement than LVEF for follow-up of LV systolic function by multiple observers.[8] In contrast, assessment of regional LV longitudinal strain has shown higher inter-vendor variability.[9] Differences in image quality, tracking algorithms, and noise reduction by temporal and spatial smoothing across the various vendors may explain the high variability in regional strain measurements. Reproducible measurements of LV GLS and regional strain are important when echocardiographic follow-up is needed. In patients undergoing cancer treatment, early detection of cardiac dysfunction is the key to implement cardioprotective strategies to prevent irreversible cardiotoxicity. Left ventricular strain and strain rate measurements are more sensitive markers of LV systolic dysfunction than LVEF, which may enable earlier detection of cardiac damage. How these measures relate to ventricular-arterial coupling in this particular subgroup of patients was evaluated by Narayan *et al.*[10] Of 135 patients with breast cancer receiving doxorubicin and trastuzumab, 15% developed cancer therapeutics-related cardiotoxicity over a median follow-up of 1.9 years. The ratio between effective arterial elastance and the end-systolic elastance (measure of ventricular-arterial coupling) and LV circumferential strain at baseline showed the largest area under the curve (AUC) to predict the occurrence of cancer therapeutics-related cardiotoxicity (0.703 and 0.655, respectively). However, these areas under the curve indicate the modest discriminatory ability to identify the patients who will develop cardiotoxicity. Randomized clinical trials would be ideal to determine the external validity of these findings.

Nuclear imaging

Nuclear imaging provides unique, additional information to that provided by other imaging techniques. However, nuclear imaging involves ionizing radiation. In a recent consensus document by the three major European professional as-

što manju dozu zračenja.[11] Na polju nuklearne kardiologije, uporaba novih kadmiji-cink-telurij gama-kamera (koje pružaju povećanu efikasnost u detekciji signala) i tehnologije digitalne pozitronske emisijske tomografije (PET) temeljene na silikonskim fotomultiplikatorima rezultirali su znatnim smanjenjem zračenja kojem su bolesnici izloženi (količina je zračenja usporediva s količinom zračenja kojom su ljudi prirodno izloženi) bez znatnog utjecaja na kvalitetu slike i dijagnostičku točnost.

Nuklearno perfuzijsko oslikavanje i kompjutorizirana tomografska angiografija miokarda (CCTA) daju važne prognostičke informacije. Povezanost između osobina aterosklerotskih plakova na CCTA te prisutnost ishemije miokarda na ^{99m}Tc-tetrofosmin jednofotonskoj emisijskoj kompjutoriziranoj tomografiji (SPECT) u naporu/odmoru procijenjena je u 184 bolesnika s jednožilnom CAD.[12] Ukupni volumen plaka i opterećenje, a posebno za nekalcificirane plakove, nekalcificirane plakove niske gustoće i kalcificirane plakove, indeks pregradnje, razlika u gustoći kontrasta, duljina lezije te promjer stenoze bili su mnogo veći u onih koronarnih arterija koje su na perfuzijskim slikama miokarda vodile u ishemična područja u usporedbi s arterijama koje su vodile u neishemična područja. Međutim, na multivarijatnoj analizi, nekalcificirani plakovi (OR 2.6), nekalcificirani plakovi niske gustoće (OR 3.9) te razlika u gustoći kontrasta (OR 2.7) bili su znatno povezani s ishemijom, ali ne i stupnjem stenoze. Ova je studija je pokazala su druga obilježja plakova, a ne samo suženje lumena koronarnih arterija, glavne odrednice ishemije miokarda. Rezultati donose zanimljivu potporu koncepciji da na ishemiju utječe vulnerabilnost plakova, a ne samo suženje lumena.

Sarkoidoza srca ostaje jedan od velikih dijagnostičkih izazova u kardiologiji. Kardiovaskularna magnetna rezonancija (CMR) i PET sve se više primjenjuju za otkrivanje zahvaćenosti srca u sarkoidozi. Oslikavanje aktivne sarkoidoze PET-om temelji se na detekciji upale miokarda koristeći se ^{18}F-florodeoksiglukozom (FDG). Međutim, unos ^{18}F-FDG-a nije specifičan za sarkoidozu. Iako se provodi posebna priprema bolesnika kako bi se minimiziralo iskorištavanje glukoze u miokardu, određeni fiziološki unos ^{18}F-FDG-a normalno je prisutan u srcu. Schildt *i sur.*[13] dokazali su dijagnostičku točnost heterogenosti miokardnog unosa ^{18}F-FDG-a u 271 uzastopnog bolesnika sa sumnjom na sarkoidozu srca upućenog na PET kompjutoriziranu tomografiju (CT). Kvantificirajući maksimum, minimum, srednju vrijednost i standardnu devijaciju vrijednosti segmentalnog unosa ^{18}F-FDG u svakome od 17 segmenata LV, izračunan je koeficijent varijacije cijelog LV-a kao prosjek svake segmentalne standardne devijacije podijeljene s prosjekom svake segmentalne srednje vrijednosti. Taj koeficijent varijacije mjera je metaboličke heterogenosti LV-a. Istraživači su predložili 0,184 kao graničnu vrijednost za detekciju sarkoidoze srca (75 %-tna osjetljivost, 51,4 %-tna specifičnost).

PET s ^{18}F-fluorodeoksiglukozom postao je jedna od standardnih slikovnih metoda u bolesnika sa sumnjom na endokarditis.[14] Prije je dokazano da PET pruža važne dijagnostičke podatke u bolesnika sa sumnjom na endokarditis bioproteza. Nasuprot tomu, osjetljivost ^{18}F-FDG PET-a niska je pri endokarditisu nativnih valvula ako nije zahvaćen i valvularni prsten ili postoji žarište infekcije izvan miokarda. Malo je informacija dostupno o fiziološkom unosu ^{18}F-FDG-a pri endokarditisu bioproteza. Mathieu *i sur.*[15] karakterizirali su obrasce unosa ^{18}F-FDG-a u bolesnika s bioprotezama bez infekcije.

sociations in the field of cardiac imaging, the best practices (technology, radiotracers, and data acquisition) to achieve the lowest radiation were summarized.[11] In the field of nuclear cardiology, the use of new cadmium–zinc–telluride gamma cameras (that provide increased signal detection efficiency) and digital positron emission tomography (PET) detector technology based on silicon photomultipliers have resulted in a significant decrease in patient radiation burden (comparable to natural radiation exposure) without major impact on image quality and diagnostic accuracy.

Both nuclear perfusion imaging and coronary computed tomography angiography (CCTA) provide important prognostic information. The association between atherosclerotic plaque features on CCTA and the presence of myocardial ischaemia on ^{99m}Tc-tetrofosmin stress/rest single photon emission computed tomography (SPECT) was evaluated in 184 patients with single vessel CAD.[12] Total plaque volume and burden, and specifically for non-calcified, low-density non-calcified and calcified plaques, remodelling index, contrast density difference, lesion length, and diameter stenosis were significantly larger in those coronary arteries supplying ischaemic territories on myocardial perfusion imaging as compared with arteries supplying non-ischaemic territories. However, on multivariable analysis, non-calcified plaques (odds ratio 2.6), low-density non-calcified plaques (odds ratio 3.9) and contrast density difference (odds ratio 2.7) were significantly associated with ischaemia, whereas the degree of stenosis was not. The study demonstrated that other plaque characteristics than only coronary luminal narrowing are major determinants of myocardial ischaemia. These results provide interesting support for the concept that ischaemia reflects not only luminal narrowing but also relates to vulnerable plaques.

Cardiac sarcoidosis remains one of the major diagnostic challenges in cardiology. Cardiovascular magnetic resonance (CMR) and PET imaging are increasingly used to detect cardiac involvement of sarcoidosis. Imaging of active sarcoidosis with PET is based on detection of myocardial inflammation using ^{18}F-fluorodeoxyglucose (FDG). However, ^{18}F-FDG uptake is not specific for sarcoidosis. Although special patient preparation is applied to minimize myocardial glucose utilization, some degree of physiological ^{8}F-FDG uptake is commonly present in the heart. Schildt *et al.*[13] demonstrated the diagnostic accuracy of heterogeneity of myocardial ^{18}F-FDG uptake in 271 consecutive patients with suspected cardiac sarcoidosis referred for PET-computed tomography (CT). By quantifying the maximum, minimum, mean, and standard deviation of the segmental, ^{18}F-FDG uptake values of each of the 17 LV segments, the coefficient of variation of the entire left ventricle was calculated as the average of each segmental standard deviation divided by the average of each segmental mean. This coefficient of variation is a measure of LV metabolic heterogeneity. The investigators proposed a cut-off value of 0.184 to have the best accuracy to detect cardiac sarcoidosis (75% sensitivity, 51.4% specificity).

^{18}F-fluorodeoxyglucose PET has become one of the standard imaging tests in patients with suspected endocarditis.[14] It has been shown earlier that PET provides important diagnostic information in patients with suspected prosthetic valve endocarditis. In contrast, the sensitivity of ^{18}F-FDG PET is low in native valve endocarditis if no annular involvement or extra-cardiac infection focus exist. In prosthetic valve endocarditis, relatively little information is available about the physi-

Autori su identificirali 54 bioproteze bez endokarditisa koje su oslikane PET-om s ^{18}F-FDG-om. Određeni stupanj unosa FDG-a prisutan je u perivalvularnom području bioproteza. Unos radiofarmaka procijenjen kvantitativnom analizom bio je znatan u mnogih bolesnika te nešto viši kod mehaničkih nego kod bioloških valvula (standardizirana vrijednost unosa 4,0 [2,4–8,0], odnosno 3.3 [2.1 – 6,1] Međutim, uzorak je tipično bio homogen. Stoga pri dijagnostici endokarditisa bioproteza nije važan kriterij samo intenzitet unosa ^{18}F-FDG-a nego je bitna i heterogenost. Dell'Aquila *i sur.*[16] dokazali su da je kvantitativni ^{18}F-FDG PET-CT optimalni dijagnostički alat u detekciji površinskih i dubinskih infekcija *driveline* u bolesnika sa zatajivanjem srca kod kojih je ugrađena mehanička potpora LV kontinuiranog protoka. Nasuprot tomu, točnost je kvantitativnog ^{18}F-FDG PET-CT u dijagnostici injekcija kućišta pumpe ograničena te je potreban kvalitativni pristup u kombinaciji s kliničkim pokazateljima (**slika 1B**). Osim za navedeno, ^{18}F-FDG PET se sve više rabi za dijagnostiku infekcija kardijalnih implantabilnih elektroničkih uređaja. *Juneau i sur.*[17] napravili su sistematski pregled i metaanalizu točnosti PET-a i SPECT-a u detekciji infekcija kardijalnih implantabilnih elektroničkih uređaja. Ukupno 13 članaka (11 studija s upotrebom ^{18}F-FDG PET-CT-a i 2 studije s upotrebom scintigrafije označenim leukocitima) zadovoljilo je uključne kriterije. Udružena osjetljivost ^{18}F-FDG PET-CT-a u dijagnostici infekcija kardijalnih implantabilnih elektroničkih uređaja bila je 87 % (95 % CI 82 % – 91 %), a udružena je specifičnost bila 94 % (95 % CI 88 % – 98 %). Analiza ROC krivulja pokazala je dobru cjelokupnu točnost s AUC od 0,935. Za scintigrafiju označenim leukocitima, obje su

ological ^{18}F-FDG uptake. Mathieu *et al.*[15] characterized ^{18}F-FDG uptake patterns in non-infected prosthetic heart valves. The authors identified 54 prosthetic valves without endocarditis that have undergone ^{18}F-FDG PET imaging. Some degree of peri-prosthetic FDG uptake was present in majority of prosthetic valves. The tracer uptake using quantitative analysis was significant in many patients and somewhat greater in mechanical than in biological valves (standardized uptake value 4.0 [2.4–8.0] and 3.3 [2.1–6.1], respectively). However, the pattern was typically homogeneous. Therefore, not only the intensity of ^{18}F-FDG uptake but also its heterogeneity is the important criteria for prosthetic valve endocarditis. Furthermore, Dell'Aquila *et al.*[16] demonstrated that quantitative ^{18}F-FDG PET-CT is an optimal diagnostic tool to detect superficial and deep driveline infections in heart failure patients recipients of continuous flow LV assist device. In contrast, the accuracy of quantitative ^{18}F-FDG PET-CT to diagnose pump housing infection is limited and a qualitative approach together with the clinical information should be considered in this situation (**Figure 1B**). In addition, ^{18}F-FDG PET is increasingly used for the diagnosis of cardiac implantable electronic device infection. Juneau *et al.*[17] performed a systematic review and meta-analysis of the accuracy of PET and SPECT to detect cardiac implantable electronic device infection. A total of 13 articles (11 studies for ^{18}F-FDG PET-CT and 2 for labelled leucocyte scintigraphy) met the inclusion criteria. The pooled sensitivity of ^{18}F-FDG PET-CT for the diagnosis of cardiac implantable electronic device infection was 87% (95% CI 82%–91%) and pooled specificity was 94% (95% CI 88%–98%).

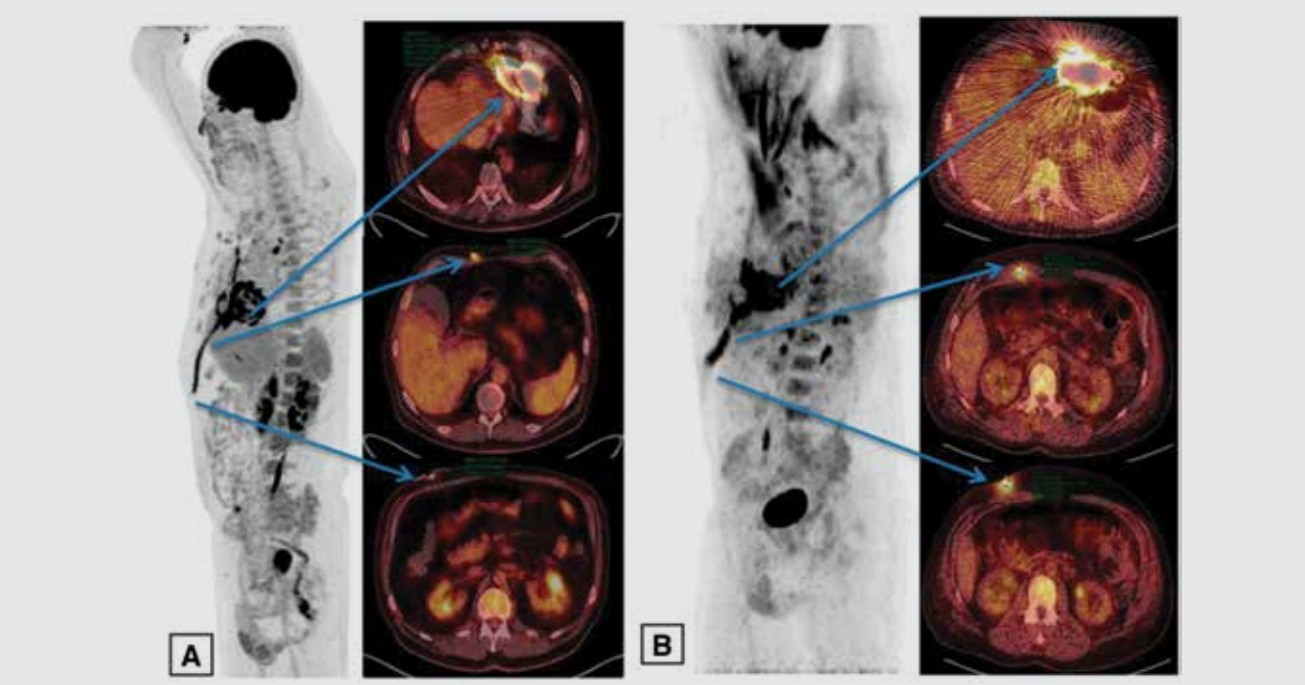

FIGURE 1B. ^{18}F-fluorodeoxyglucose positron emission tomography–computed tomography to diagnose left ventricular assist device infection. On maximum intensity projections and fused transaxial positron emission tomography–computed tomography images, the pathological uptake of ^{18}F-fluorodeoxyglucose is visualized at the piercing site of the driveline and along the intracorporeal course in panel *A* whereas panel *B* shows pathological ^{18}F-fluorodeoxyglucose accumulation at all the levels including the pump housing. Reproduced with permission from Dell'Aquila *et al.*[16]

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studije pokazale senzitivnost od 90 % i specifičnost od 100 %. Autori su zaključili da ^{18}F-FDG PET-CT i scintigrafija označenim leukocitima pokazuju visoku osjetljivost, specifičnost i točnost, ali je u slučaju scintigrafije dostupno malo podataka. Autori kao metodu izbora preporučuju ^{18}F-FDG PET ako je dostupna. Također, scintigrafija označenim leukocitima čini se kao koristan alat za dijagnostiku infekcija kardijalnih implantabilnih elektroničkih uređaja.

Kardiovaskularna magnetna rezonancija

Među ustaljenim kliničkim primjenama za CMR, mjerenje miokardnog opterećenja željezom postalo je sastavni dio liječenja bolesnika s talasemijom major te je terapija vođena CMR-om znatno smanjila smrtnost u ovoj skupini bolesnika. U nedavnoj kohorti od 481 bolesnika s talasemijom na suvremenoj terapiji Pepe *i sur.*[18] opisali su koji su nalazi na CMR-u neovisno povezani s pojavnošću zatajivanja srca i aritmijama. Ukupno, učestalost neželjenih ishoda bila je niska jer se samo u 16 bolesnika razvilo srčano popuštanje, a u 16 bolesnika manifestiralo aritmijama tijekom praćenja od 6 godina. Fibroza miokarda na kasnom pojačanju gadolinijem (LGE) CMR je povezana s neželjenim ishodima (HR = 10,9, P < 0,001), homogenim preopterećenjem miokarda željezom (HR = 5,6, P = 0,016) i ventrikulskom disfunkcijom (HR = 4,33, P = 0,011). Terapija kelatorima željeza je promijenjena u gotovo 70 % bolesnika kao rezultat CMR studije, što upućuje na kliničku značajnost CMR-a u ovoj bolesti.

Prognostička značajnost LGE CMR-a također je bila predmet nekoliko metaanaliza i studija jednog centra u čestim i rijetkim bolestima. Raina *i sur.*[19] saželi su prognostičku vrijednost LGE-a iz 7 studija s 425 bolesnika sa sustavnom amiloidozom. Bolesnici s dokazanom fibrozom na LGE CMR-u imali su gotovo pet puta višu smrtnost nakon prosječnog razdoblja praćenja od 25 mjeseci u usporedbi s onima bez LGE-a (udruženi OR 4,96; 95 % CI 1,90 – 12,93; P = 0,001). U bolesnika sa sarkoidozom Coleman *i sur.*[20] udružili su rezultate 10 studija s ukupno 760 bolesnika. Prisutnost LGE-a povezana je s trostrukim povećanjem ukupne smrtnosti nakon 3,0 ± 1,1 godinu i deseterostrukim povećanjem složenih ishoda koji su također uključivali ventrikulske aritmije, šokove ugradbenih kardioverterskog defibrilatora i iznenadne srčane smrti. U velikoj studiji provedenoj u jednom centru Halliday *i sur.*[21] prikazali su podatke 399 bolesnika s dilatativnom kardiomiopatijom i LVEF ≥40 %. Bolesnici su podvrgnuti CMR-u, uključujući i LGE te su praćeni u medijanu od 4,6 godina. Prisutnost fibroze srednjeg zida na LGE-u je povezana s 9,2 puta povećanim rizikom od složenih ishoda iznenadne smrti i zaustavljene iznenadne smrti, peterostrukim povećanjem rizika od iznenadne srčane smrti i 35 puta povećanim rizikom od zaustavljene iznenadne srčane smrti. Manja studija koju su u jednom centru proveli Pendrotti *i sur.*[22] istražila je prognostičku vrijednost LGE-a u 48 bolesnika s ortotopičnom transplantacijom srca. Najsnažniji prediktor značajnih neželjenih kardiovaskularnih događaja jest vaskulopatija alografta miokarda (HR 3,63, P = 0,004), potom masa LGE-a (HR 1,04, P = 0,0007) i postotak LGE-a u masi LV-a (HR 1,083, P = 0,0002). Ove metaanalize i studije provedene u jednom centru pridodaju skupu dokaza koji podupiru uporabu LGE CMR-a kao važnog markera neželjenih kliničkih događaja u širokom spektru bolesti.

Potencijalnu primjenu LGE CMR-a u liječenju AF-a istražili Gal i Marrouche.[23] LGE CMR može rabiti u karakterizaciji fi-

The receiver operating characteristics curve analysis demonstrated good accuracy overall, with an AUC of 0.935. For labelled leucocyte scintigraphy, both studies reported sensitivity above 90% and specificity of 100%. The authors concluded that both ^{18}F-FDG PET-CT and leucocyte scintigraphy yield high sensitivity, specificity, and accuracy, but limited data is available on the latter. The authors recommended to use ^{18}F-FDG PET as preferred method when available. Also leucocyte scintigraphy appears useful tool for the diagnosis of cardiac implantable electronic device infection.

Cardiovascular magnetic resonance

Among the established clinical applications of CMR, the measurement of cardiac iron loading has become an integral part of the management of patients with thalassaemia major and CMR guided management has dramatically reduced mortality in this patient population. In a recent cohort of 481 thalassaemia patients on contemporaneous treatment, Pepe *et al.*[18] described which CMR findings are independently associated with the occurrence of heart failure and arrhythmias. Overall, the rate of adverse outcomes was low with only 16 patients experiencing heart failure and 16 presenting with an arrhythmia during 6 years follow-up. Myocardial fibrosis on late gadolinium enhancement (LGE) CMR was associated with adverse outcomes (HR = 10.9, $P < 0.001$), homogeneous myocardial iron overload (HR = 5.6, $P = 0.016$) and ventricular dysfunction (HR = 4.33, $P = 0.011$). Iron chelation management was changed in nearly 70% of patients as a result of the CMR study, underlining the clinical relevance of CMR in this condition.

The prognostic relevance of LGE CMR has also been the subject of several meta-analyses and single-centre studies in common and more rare diseases. Raina *et al.*[19] summarized the prognostic value of LGE from 7 studies with 425 systemic amyloidosis patients. Patients with evidence of fibrosis on LGE CMR had almost five times higher mortality at a mean follow-up of 25 months compared to those without LGE (pooled odds ratio: 4.96; 95% CI 1.90-12.93; $P = 0.001$). In sarcoidosis, Coleman *et al.*[20] pooled the results of 10 studies with a total of 760 patients. The presence of LGE was associated with a three-fold increase in all-cause mortality at 3.0 ± 1.1 years and a 10-fold increase in a composite endpoint that also included ventricular arrhythmia, implantable cardioverter defibrillator shocks, and sudden cardiac death. In a large single-centre study, Halliday *et al.*[21] presented data on 399 patients with dilated cardiomyopathy and LVEF ≥ 40%. Patients underwent CMR including LGE and were followed-up for a median of 4.6 years. The presence of mid-wall fibrosis on LGE was associated with a 9.2-fold increase in the risk of a composite endpoint of sudden death and aborted sudden death, a five-fold increase in the risk of sudden cardiac death alone and a 35-fold increase in the risk of aborted sudden cardiac death. A smaller single-centre study by Pedrotti *et al.*[22] examined the prognostic value of LGE in 48 patients with orthotopic heart transplantation. The strongest predictor of major adverse cardiovascular events was cardiac allograft vasculopathy (HR 3.63, $P = 0.004$) followed by LGE mass (HR 1.04, $P = 0.0007$) and percentage of LGE of LV mass (HR 1.083, $P = 0.0002$). These meta-analyses and single-centre studies add to the expanding evidence supporting the use of LGE CMR as a strong marker of adverse clinical outcome in a wide range of diseases.

The potential applications of LGE CMR in the management of AF were reviewed by Gal and Marrouche.[23] Late gadolinium

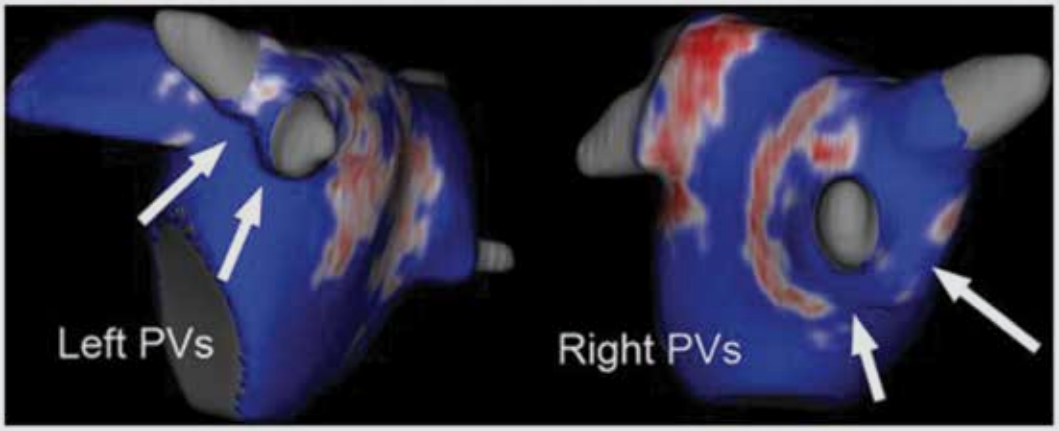

FIGURE 2. Late gadolinium enhanced cardiovascular magnetic resonance images of the left atrium following pulmonary vein ablation for atrial fibrillation. The arrows point to gaps in the pulmonary vein encirclement. Reproduced with permission from Gal and Marrouche.[23]

PV, pulmonary vein.

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broze LA kao prediktora vraćanja AF-a, kao vodiča postablacijskog uspjeha (**slika 2**). Osim toga, Csepe *i sur.*[24] izvijestili su da se LGE može primjenjivanja u vizualizaciji zdravoga ljudskoga sinoatrijalnog čvora, koji se sastoji od 35 – 55 % fibroznoga tkiva okružena masnim tkivom, pružajući mehaničku i električnu zaštitu od okolnoga tkiva atrija. Koristeći se visoko rezolucijskim 3T CMR-om, sinoatrijalni se čvor vizualiziran u četiri zdrava dobrovoljca i optički prikazan s 9,4 T kontrastno poboljšane CMR kod pet eksplantiranih donorskih srca (**slika 3**). Nalazi CMR-a usko su povezani s histološkim nalazima. Kombinirano s LGE-om LA, identifikacija lokacije sinoatrijskoga čvora mogla bi unaprijediti primjenu CMR-a u bolesnika s AF-om i pomoći u provođenju još bolje ciljane ablacije.

Dok LGE ima jedinstvenu sposobnost detekcije fokalne fibroze i ožiljka, T1 mapirajući CMR omogućuje otkrivanje i kvantifikaciju difuznih procesa miokarda poput upale i fibroze. Liu *i sur.*[25] napravili su nativno T1 mapiranje kao dio sveobuhvatnog CMR protokola u 61 bolesnika s infarktom miokarda uz elevacijom ST-segmenta (STEMI) i pokazali da različite pragovi T1 vrijednosti mogu razlikovati reverzibilnu i ireverzibilnu ozljedu miokarda. Volumen oštećenja miokarda utvrđen uporabom pragova nativne T1 sekvencije korelirao je i s otpuštanjem troponina I i sa šestomjesečnom LVEF kao markerom remodeliranja LV-a. U slično dizajniranoj studiji Garg *i sur.*[26] kombinirali nativne i postkontrastno poboljšane CMR snimke kako bi kvantificirali frakciju izvanstaničnog volumena miokarda u 50 bolesnika koji su bili podvrgnuti CMR-u 24 – 72 sata nakon akutnog infarkta miokarda te 3 mjeseca poslije. Frakcija izvanstaničnog volumena mjerena 24 – 72 sata nakon akutnog infarkta miokarda korelirala je sa segmentima koji su pod rizikom (procijenjenim T2 CMR sekvencijama) te konačnom veličinom infarkta procijenjenom nakon 3 mjeseca LGE-om. Na kraju su Reinstadler *i sur.*[27] istražili nativne T1 sekvencije u udaljenoj zoni miokarda koja nije zahvaćena infarktom u 225 bolesnika sa STEMI-jem. Nađene su povišene nativne T1 vrijednosti u udaljenim zonama u bolesnika s opširnijim infarktima, manje očuvanog miokar-

enhancement CMR can be used to characterize LA fibrosis as a predictor of AF recurrence, as a guide to post-ablation success (**Figure 2**). Furthermore, Csepe *et al.*[24] reported that LGE can even be used to visualise the healthy human sinoatrial node, which consists of 35–55% fibrotic tissue surrounded by fatty tissue, providing mechanical and electrical protection from the surrounding atrial tissue. Using high-resolution 3 T CMR, the sinoatrial node was visualized in four healthy volunteers and optically mapped with 9.4 T contrast-enhanced CMR in five explanted donor hearts (**Figure 3**). The CMR findings correlated closely with the findings from the histological sections. Combined with LGE of the LA, identification of the sinoatrial node location may further enhance the use of CMR in patients with AF and help to perform a more targeted ablation procedure.

While LGE is uniquely able to detect focal fibrosis and scar, T1 mapping CMR allows the detection and quantification of diffuse myocardial processes such as inflammation and fibrosis. Liu *et al.*[25] performed native T1 mapping as part of a comprehensive CMR protocol in 61 STEMI patients and showed that different thresholds of T1 values can differentiate between reversible and irreversible myocardial injury. The volume of myocardial damage using a native T1 threshold correlated with both troponin I release and 6 months of LVEF as a marker of LV remodelling. In a similar study design, Garg *et al.*[26] combined both native and post-contrast enhanced CMR to quantify the myocardial extracellular volume fraction in 50 patients who underwent CMR acutely (24–72 h) after infarction and at 3 months of follow-up. Extracellular volume fraction acutely measured post-infarction correlated with the area at risk (assessed with T2-weighted CMR sequences) and final infarct size by LGE at 3 months. Finally, Reinstadler *et al.*[27] investigated native T1 in the non-infarcted remote zone in 225 ST-segment elevation myocardial infarction (STEMI) patients. Elevated native T1 values in the remote zone were noted in patients with larger infarcts, less myocardial salvage and worse LV function at baseline. In multivariable analysis,

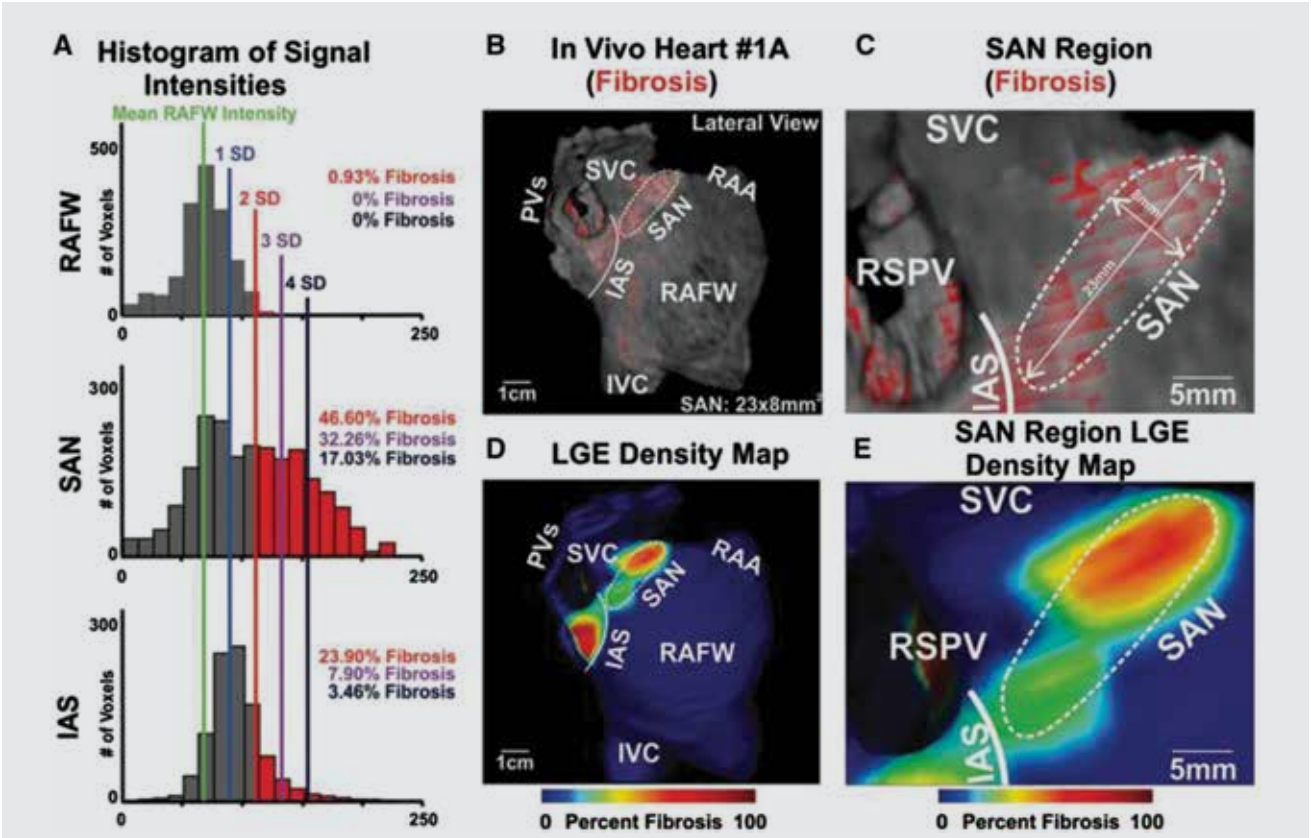

FIGURE 3. Late gadolinium contrast enhanced cardiovascular magnetic resonance to identify the sinoatrial node. Panel A displays the histograms of total signal intensity of the right atrial free wall, sinoatrial node, and interatrial septum. To determine the percentage of fibrosis, the mean signal intensity of the right atrial free wall is considered the reference. Each standard deviation above the mean signal intensity of the right atrial free wall indicates increasing fibrosis. The lateral view of the three-dimensional reconstruction of the right atrium is presented in panel B. The red-shaded area indicates the sinoatrial node, demarcated by a white dashed line, and its dimensions are shown in a zoomed view in panel C. The density maps of the right atrium and the zoomed view of the sinoatrial node are displayed in panels D and E, respectively. Reproduced with permission from Csepe *et al*.[24]

IAS, interatrial septum; IVC, inferior vena cava; PVs, pulmonary veins; RAA, right atrial appendage; RAFW, right atrial free wall; RSPV, right superior pulmonary vein; SAN, sinoatrial node; SVC, superior vena cava; SD, standard deviation.

da i lošijom funkcijom LV-a pri prvom pregledu. U multivarijatnoj analizi nativne T1 vrijednosti udaljenih zona bile su neovisno povezane s značajnim neželjenim kardiovaskularnim događajima. Kombinirajući nativne T1 vrijednosti udaljene zone s ostalim poznatim prognostičkim CMR markerima (LVEF, opsežnost infarkta te indeks spašavanja miokarda), postignuto je poboljšanje netoreklasifikacije od 0,82 (95 % CI 0,46–1,17; P < 0,001). Ovi nalazi upućuju na to da karakteristike udaljene zone u bolesnika sa STEMI-jem mogu imati kliničku značajnost te da bi nativno T1 mapiranje moglo biti upotrijebljeno u poboljšanju stratifikacije rizika.

Multiparametrijskim CMR-om mogu se okarakterizirati kompleksni fiziološki procese *in vivo*. Levelt *i sur*.[28] procjenjivali su 31 dijabetičara tipa II bez CAD-a i 17 podudarnih kontrola s adenozinskim stresnim CMR-om kako bi dobili polukvantitativni indeks rezervne perfuzije miokarda, oslikavanjem ovisnom o koncentraciji kisika u krvi, koji mjeri oksigenaciju miokarda i MR spektroskopiju omjera kreatin-fosfata i adenonative T1 values of the remote zone were independently associated with major adverse cardiac events. Adding the native T1 values of the remote zone to other known prognostic CMR markers (LVEF, infarct size, and myocardial salvage index) led to a net reclassification improvement of 0.82 (95% CI 0.46–1.17; $P < 0.001$). These findings suggest that remote zone characteristics in patients with STEMI may have clinical relevance and that native T1 mapping could be used to improve risk stratification.

Multi-parametric CMR can characterize complex physiological processes *in vivo*. Levelt *et al*.[28] evaluated 31 patients with type 2 diabetes mellitus without CAD and 17 matched controls with adenosine stress CMR to derive a semi-quantitative myocardial perfusion reserve index, blood-oxygen level-dependent imaging, which measures myocardial oxygenation, and MR spectroscopy of the phosphocreatine to adenosine tri-phosphate (PCr/ATP) ratio to study myocardial energy handling. Data were acquired at rest and during

zin trifosfata (PCr/ATP) kako bi istražili upravljanje energijom u miokardu. Podatci su dobiveni tijekom mirovanja i u naporu. Pri prvom pregledu dijabetičari su imali 17 % niži PCr/ATP omjer u usporedbi s kontrolnom populacijom, što upućuje na prisutnost oštećenog upravljanja energijom, koje se pogoršalo za 12 % tijekom napora. Uz sve navedeno, u tijeku vazodilatacijskoga stresa, indeks rezervne perfuzije miokarda bio je 24 % niži te je oksigenacijski odgovor u dijabetičara bio oslabljen u usporedbi s kontrolama. Ova zapažanja podupiru koncept koji kaže da disfunkcija miokardijalne mikrovaskulature u dijabetičara pogoršava rastrojstvo kardijalne energetike pod uvjetima povećanog opterećenja i naglašava potencijal multiparamertrijskog CMR-a u istraživanju kompleksnih patofizioloških procesa.

Kompjutorizirana tomografija

Kalcij u koronarnim arterijama nudi mogućnost detekcije i kvantificiranja supkliničke ateroskleroze te identifikaciju osoba s povišenim rizikom za buduće kardiovaskularne događaje. Budoff *i sur.*[29] u bolesnika niskog rizika s bolovima u prsnom košu i sumnjom na CAD uključenih u studiju PROMISE analizirali su prognostičku vrijednost kalcija u koronarnim arterijama. Ukupno 4602 bolesnika koji su podvrgnuti detekciji kalcija u koronarnim arterijama i CCTA-u uspoređena su s kohortom od 4602 bolesnika koji su bili podvrgnuti funkcijskom testiranju na ishemiju. Obje su kohorte bile praćene tijekom 26 mjeseci te su bili registrirani smrtni ishodi, infarkt miokarda i hospitalizacije zbog nestabilne angine pektoris. Sposobnost u predviđanju događaja bila slična pri mjerenju kalcija u koronarnim arterijama i pri funkcijskom testiranju (C-statistika: 0,67 prema 0,64) – uz napomenu da je mjerenje kalcija koronarnih arterija bilo osjetljivije, dok je funkcijskog testiranje bilo specifičnije. CCTA je bio više prediktivan za događaje i od mjerenja kalcija koronarnih arterija i od funkcijskog testiranja (C-statistika: 0,72). Ovakvi rezultati naglašavaju ulogu mjerenja kalcija u koronarnim arterijama kao markera opterećenja ateroskleroze i prediktora kardiovaskularnih događaja, a kvantifikacija stenoza koronarnih arterija i karakterizacija plakova s CCTA pružaju bolju snagu diskriminacije u identifikaciji rizičnih bolesnika.

Nielsen *i sur.*[30] procjenjivali su prognostičku vrijednost klinički indicirane CCTA u velikoj kohorti od 16 949 danskih bolesnika starijih od 18 godina koji su zbog sumnje na CAD bili praćeni u razdoblju od 5 godina. Tijekom studije promatrani su složeni zajednički ishodi, od kasne revaskularizacije miokarda, infarkta miokarda te ukupne smrtnosti. Revaskularizacije koje su se dogodile unutar 90 dana od CCTA pregleda nisu uzete u obzir da bi se isključio one koje su se dogodile zbog neposrednih nalaza na CT-u. Složeni su se zajednički ishodi dogodili u 486 bolesnika tijekom medijana praćenja od 3,6 godina. Rizik od složenih ishoda bio je: 1,5 % za bolesnike bez nalaza ateroskleroze koronarnih arterija na CCTA, 3,3 % ako je bio prisutan neopstruktivni plak i 6,8 % za bolesnike s opstruktivnim lezijama na CCTA (P < 0,001 za sve, **slika 4**). Ako je bila prisutna trožilna koronarna bolest ili stenoza lijeve glavne koronarne arterije (LMCA), rizik je bio 15 %. Zanimljivo, prediktivna vrijednost CCTA održana je kroz sve dobne skupine, u muškaraca i u žena.

Snažnu prognostičku vrijednost CCTA-a također su potvrdili Deseive *i sur.*[31] Od 15 219 bolesnika uključenih u međunarodni registar CONFIRM njih 982 (6,5%) umrla su tijekom me-

exercise. At baseline, diabetic patients had a 17% lower PCr/ATP ratio compared with a control population, suggesting the presence of impaired energy handling, which worsened by 12% with exercise. In addition, during vasodilator stress, myocardial perfusion reserve index was 24% lower and oxygenation response was blunted in diabetic patients as compared to controls. These observations support the concept that coronary microvascular dysfunction in diabetes exacerbates derangement of cardiac energetics under conditions of increased workload and underline the potential of quantitative multi-parametric CMR to study complex pathophysiological processes.

Computed tomography

Coronary calcium offers a possibility to detect and quantify subclinical atherosclerosis and identify individuals at increased risk for future cardiovascular events. In low-risk patients with chest pain and suspected CAD included in the Prospective Multicenter Imaging Study for Evaluation of Chest Pain (PROMISE) trial, Budoff *et al.*[29] analysed the prognostic value of coronary calcium. A total of 4602 patients who underwent coronary calcium imaging and CCTA were compared to a cohort of 4602 individuals who underwent functional ischaemia testing. Both cohorts were followed for 26 months and the occurrence of all-cause death, myocardial infarction, or unstable angina hospitalization was recorded. Overall, the ability to predict events was similar for coronary calcium and functional testing (C-statistic: 0.67 vs. 0.64)—with coronary calcium being more sensitive and functional testing being more specific. Interestingly, CCTA was significantly more predictive for events than both calcium and functional testing (C-statistic: 0.72). These results underscore the role of coronary calcium as marker of atherosclerosis burden and predictor of cardiovascular events but quantification of coronary stenosis and plaque characterization with CCTA provide better discriminatory power to identify patients at risk.

The prognostic value of clinically indicated CCTA was evaluated in a large cohort by Nielsen *et al.*[30] In a region of Denmark, 16 949 patients older than 18 years who underwent CCTA for suspected CAD were systematically followed for the occurrence of a composite endpoint of late myocardial revascularization, myocardial infarction, and all-cause death during a 5 years' period. Revascularizations occurring within 90 days of CCTA were censored to exclude those that were triggered by the immediate CT findings. The composite endpoint occurred in 486 patients during a median follow-up period of 3.6 years. The risk of the composite endpoint was 1.5% for patients without identification of any coronary atherosclerosis on CCTA, 3.3% if non-obstructive plaque was present, and 6.8% for individuals with obstructive lesions in CCTA ($P < 0.001$ for all, **Figure 4**). If 3-vessel disease or left main stenosis was present, the risk was 15%. Interestingly, the predictive value of CCTA was maintained across all age groups, both in men and women.

The strong prognostic value of CCTA was also confirmed by Deseive *et al.*[31] Of 15 219 patients included in the international multicentre CONFIRM registry, 982 (6.5%) died during a median follow-up period of 5.3 years. The so-called CONFIRM score,[32] which combines the National Cholesterol Education Program Adult Treatment Panel (NCEP ATP) III score, the presence of proximal coronary artery segments contain-

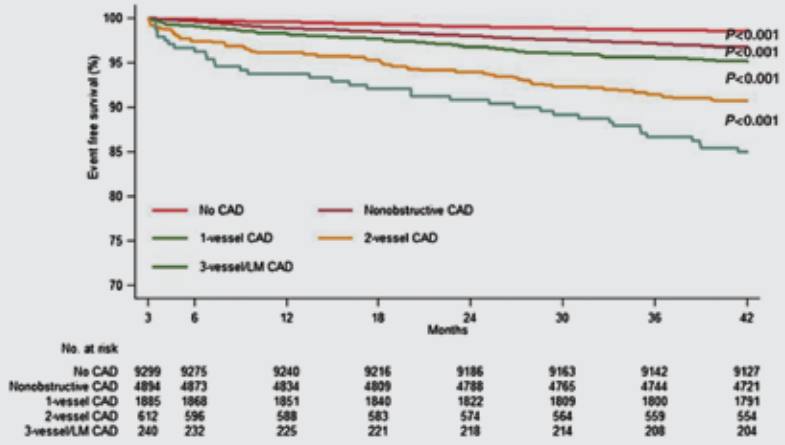

FIGURE 4. Unadjusted event-free survival from the composite endpoint according to the extent of coronary artery disease. Composite endpoint comprising late coronary revascularization, myocardial infarction, and all-cause death. Reproduced with permission from Nielsen *et al.*[30]

CAD, coronary artery disease.

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dijana praćenja od 5,3 godine. Takozvana CONFIRM bodovna skala[32] koja kombinira NCEP ATP III ljestvicu, prisutnost plaka u proksimalnim segmenima koronarnih arterija te prisutnost >50 % stenoza proksimalnih segmenata koronarnih arterija, imao je superiorniju prognostičku vrijednost od kliničkih bodovnih sustava, uključujući NCEP ATP III, Framinghamsku i Morisevu ljestvicu (C-statistika: 0,696, odnosno 0,675, odnosno 0,610, odnosno 0,606). Primjena CONFIRM ljestvice dovela je do reklasifikacije 34 % bolesnika u usporedbi sa primjenom samo NCEP ATP III sustava.

Novi, zanimljivi pristup stratifikaciji rizika utemeljen na CCTA-u opisali su Motwani *i sur*[33]. Strojno je učenje primijenjeno za stvaranje modela iz kliničkih podataka i CCTA na ukupno 10 030 bolesnika uključenih u registar CONFIRM. Primijenjeno je 25 kliničkih varijabli (godine, spol, Framinghamska bodovna skala i slično) te 44-CCTA – izvedenih parametara (ljestvica rizika segmentnih stenoza, ljestvica obuhvatnosti segmenta, modificirani Dukeov indeks, broj nekalcificiranih segmenata, miješani ili kalcificirani plakovi…). Strojno učenje automatski je odabralo svojstva, izgradilo model i križno validiralo algoritmom. Tijekom praćenja ishoda kroz prosječno 5,4 godine, umrlo je ukupno 745 bolesnika. S pomoću strojnog učenja postignut je viši AUC u usporedbi s Framinghamskom ljestvicom rizika ili bilo kojim CCTA-izvedenim sustavom bodovanja za procjenu ozbiljnosti (kao što je bodovanje obuhvatnosti segmenta u stenozi) za predviđanje ukupnog mortaliteta (strojno učenje: 0,79; Framinghamska ljestvica rizika: 0,61, ljestvica obuhvatnosti segmenta: 0,64; P < 0,001). Može se zaključiti da strojno učenje ima važnu ulogu u točnom određivanju visokorizičnih bolesnika sa suspektnom CAD koji bi mogli imati korist od preventivnog liječenja.

Postoji nekoliko načina dodavanja informacija o funkciji (prepoznavanju ishemije), oslikavanju pomoću CCTA koja čini anatomsku slikovnu tehniku. Jedan je pristup FFR-CT (*fractional flow reserve*), tj. mjerenje frakcije protoka krvi koristeći se anatomskim prikazima dobivene CT-om. Drugi je naing plaque, and the presence of proximal coronary segments containing >50% stenoses, had superior prognostic value than clinical risk scores, including the NCEP ATP III, Framingham, and Morise scores (C-statistic: 0.696, 0.675, 0.610, and 0.606, respectively). Application of the CONFIRM score led to reclassification of 34% of patients when compared with the NCEP ATP III score alone.

An interesting new approach to risk stratification based on CCTA was described by Motwani *et al.*[33] Machine learning was applied to build a model from clinical data and CCTA of 10 030 patients included in the CONFIRM registry. Twenty-five clinical variable (such as age, gender, and Framingham risk score) and 44 CCTA-derived parameters (such as segment stenosis score, segment involvement score, modified Duke index, number of segments with non-calcified, mixed or calcified plaques). Machine learning involved automated feature selection, model building, and 10-fold stratified cross-validation. During a mean follow-up of 5.4 years, 745 patients died. Machine learning yielded a higher AUC compared with the Framingham risk score or any single CCTA-derived severity scores alone (such as the segment involvement score) for predicting all-cause mortality (machine learning: 0.79; Framingham Risk Score: 0.61; segment involvement score: 0.64; $P < 0.001$). These results suggest that machine learning has an important role in correctly identifying the high-risk patients with suspected CAD who may benefit from intensified preventive treatment.

There are several approaches to add functional information (identification of ischaemia) to CCTA—which is an anatomic imaging technique. One approach is fractional flow reserve (FFR)-CT, the simulation of FFR based on CT-derived anatomic data sets. The other approach is myocardial CT perfusion during adenosine stress, which requires a separate CT acquisition. Both approaches are currently being validated. Jensen *et al.*[34] evaluated whether CCTA, combined with FFR-CT if deemed necessary, would allow to safely defer invasive coro-

čin mjerenje perfuzije miokarda nakon primjene adenozina, što zahtijeva zasebnu CT tehniku. Oba su načina trenutačno u procesu validacije. Jensen *i sur.*[34] uspoređivali su CCTA kombiniranu s FFR-CT-om s invazivnim koronarnim angiogramima. Tijekom praćenja od 6 mjeseci, u jednom centru, ukupno 774 bolesnika podvrgnuto je invazivnoj koronarografiji ili CCTA te su evaluirani. Kod svih je bolesnika tijekom iduća 3 mjeseca analizirana učestalost neželjenih događaja. Prema prisutnosti tipičnih anginoznih simptoma, bolesnici su bili podijeljeni u dvije skupine: onu s niskim do srednjim rizikom (n = 593) i onu s visokim rizikom (n = 181), s prosječnom vjerojatnošću CAD-a od 31 ± 16 % za prvu skupinu i 67 ± 16 % za drugu. U 212 (28 %) bolesnika uz CT koronarografiju primijenjen je i FFR-CT. U skupini visokorizičnih i nisko do srednje rizičnih, invazivna koronarna angiografija bila je izbjegnuta u 75 % u prvoj i 91 % bolesnika u drugoj navedenoj skupini. Tijekom razdoblja praćenja od 157 ± 50 dana, zabilježeni su ozbiljni neželjeni događaji u četiri bolesnika. Neželjeni događaji nisu zabilježeni kod bolesnika u kojih invazivna angiografija nije bila učinjena zbog urednog nalaza na CT koronarografiji (sa selektivnim FFR-CT testiranjem) – što bi značilo da je CCTA uz po potrebi i kombinaciju s FFR-CT-om sigurna metoda za obustavljanje potrebe za invazivnom koronarografijom. U studiji FFR-CT (RIPCORD)[35] koja je analizirala kohortu od ukupno 200 bolesnika multicentričnim pristupom, FFR-CT metoda je dovela do promjene u predmnijevanom planu nakon učinjene CCTA u 36 % bolesnika.

Drugi pristup, perfuzija miokarda CT-om, također je u kliničkim istraživanjima. Penagaluri *i sur.*[36] proučavali su dijagnostičku vrijednost perfuzije miokarda nakon učinjene CCTA u 381 bolesnika. Orijentirana dijagnostička preciznost prema bolesniku – vrijednost definirana prema površini ispod ROC krivulje – za CCTA u žena bila je 0,83, a za CCTA s perfuzijom miokarda CT-om 0,92 (P = 0,003). Međutim, u muškaraca nije registrirana značajna razlika (0,82 prema 0,84, P = 0,29). Bit će potrebne nove studije kako bi se ocijenila optimalna klinička upotreba CT perfuzije miokarda kao slikovne metode.

CT srca nije ograničen isključivo na evaluaciju CAD-a. Kompjutorizirana tomografija ima rastuću važnost u kontekstu strukturnih intervencija, uključujući transkatetersku ugradnju aortne valvule. Nedavno je zamijećeno da transkateterske i kirurški ugrađene aortne bioproteze mogu imati HALT – *hypo-attenuated leaflet thickening* (**slika 5**)[37-40]. Klinička važnost ovoga još je uvijek nije jasna: u nekim studijama prisutnost HALT-a nije bila povezana s povećanim rizikom od moždanog udara[37,38]. Chakravarty *i sur.*[40] tvrde da je ipak postoji viši rizik od cerebralnoga ishemijskog događaja u bolesnika s HALT-om. Zanimljivo je da je studija Sondergaard *i sur.*[37] upozorila na promjenjivost HALT-a koji može progredirati u *hypo-attenuation affecting motion* (HAM) ili regredirati ili nestati. U 84 bolesnika uključenih u registar SAVORY, dva kontrolna CT-a rađena su 140 i 298 dana nakon ugradnje valvule. HALT i HAM bili su prisutni u 38,1 % i 20,2 % bolesnika u prvom pregledu i bile su visoko dinamične dok su pokazivali progresiju u 15,5 % i regresiju u 10,7 % bolesnika. Progresija je bila manje vjerojatna u bolesnika koji su bili na oralnoj antikoagulantnoj terapiji (OR 0,014, P = 0,036), ali se regresija može dogoditi i neovisno o primjeni oralnih antikoagulansa. Rezultati tih studija doveli su u pitanje trenutačne preporuke za uporabu antikoagulantne terapije u bolesnika s aortnim bioprotezama. Dodatne studije s novijim tehnikama oslikavanja

nary angiograms. Over a period of 6 months, 774 patients referred to invasive angiography or CCTA in a single centre were evaluated. Downstream testing, treatment within 3 months and adverse events were analysed. Patients were divided in two groups according to the presence of typical angina: low-intermediate-risk (*n* = 593) and high-risk (*n* = 181), with mean pre-test probabilities of CAD of 31 ± 16% and 67 ± 16%, respectively. Coronary computed tomography angiography was supplemented by FFR-CT in 212 (28%) patients. In the high- and in the low-intermediate-risk group, invasive coronary angiography could be avoided in 75% and 91% of patients. Over a mean follow-up time of 157 ± 50 days, serious clinical events occurred in four patients. No events occurred in patients in whom invasive angiography had been cancelled due to inconspicuous findings in CCTA (with selective FFR-CT testing)—indicating that CCTA, in combination with FFR-CT when deemed necessary, allows to safely defer invasive angiography. In the FFR-CT (Does Routine Pressure Wire Assessment Influence Management Strategy at Coronary Angiography for Diagnosis of Chest Pain? (RIPCORD) study,[35] which analysed a cohort of 200 patients in a multicentre approach, FFR-CT led to a change of the downstream management plan after CCTA in 36% of patients.

The second approach, CT myocardial perfusion imaging, is also under clinical investigation. Penagaluri *et al.*[36] studied the diagnostic value of CT myocardial perfusion imaging in addition to CCTA in 381 patients. Patient-based diagnostic accuracy—defined by the area under the receiver operating curve—for CCTA alone was 0.83 and for CCTA-CT perfusion was 0.92 (*P* = 0.003) in women. However, no significant difference was found in men (0.82 vs. 0.84, *P* = 0.29). Future studies will be required to assess the optimal clinical utilization of CT myocardial perfusion imaging.

Cardiac CT imaging is not limited to the evaluation of CAD. Computed tomography plays an increasingly important role in the context of structural heart interventions, including transcatheter aortic valve implantation. A recent development has been the observation that both transcatheter and surgically implanted aortic bioprosthetic valves may display 'hypo-attenuated leaflet thickening' ('HALT') (**Figure 5**).[37–40] The clinical significance of this observation, however, has been unclear: while in some studies the presence of HALT was not associated with increased risk of stroke,[37,38] Chakravarty *et al.*[40] postulate a somewhat higher rate of cerebral ischaemic events if HALT is present. Interestingly, the study by Sondergaard *et al.*[37] highlights the temporal evolution of HALT and demonstrates that HALT can progress to hypo-attenuation affecting motion (HAM) or regress and disappear. In 84 patients included in the Subclinical Aortic Valve Bioprosthesis Thrombosis Assessed With 4D CT (SAVORY) registry, two sequential CT scans were performed at 140 and 298 days after valve implantation. Hypo-attenuated leaflet thickening and HAM were present in 38.1% and 20.2% of patients in the first scan and were highly dynamic, showing progression in 15.5% and regression in 10.7% of patients. Importantly, progression was less likely among patients treated with oral anticoagulation (OR 0.014, *P* = 0.036), but regression could happen independently of the use of anticoagulants. The results of these studies have questioned current recommendations on the use of anticoagulation therapy for aortic bioprostheses. Additional studies using sequential imaging are needed to unravel

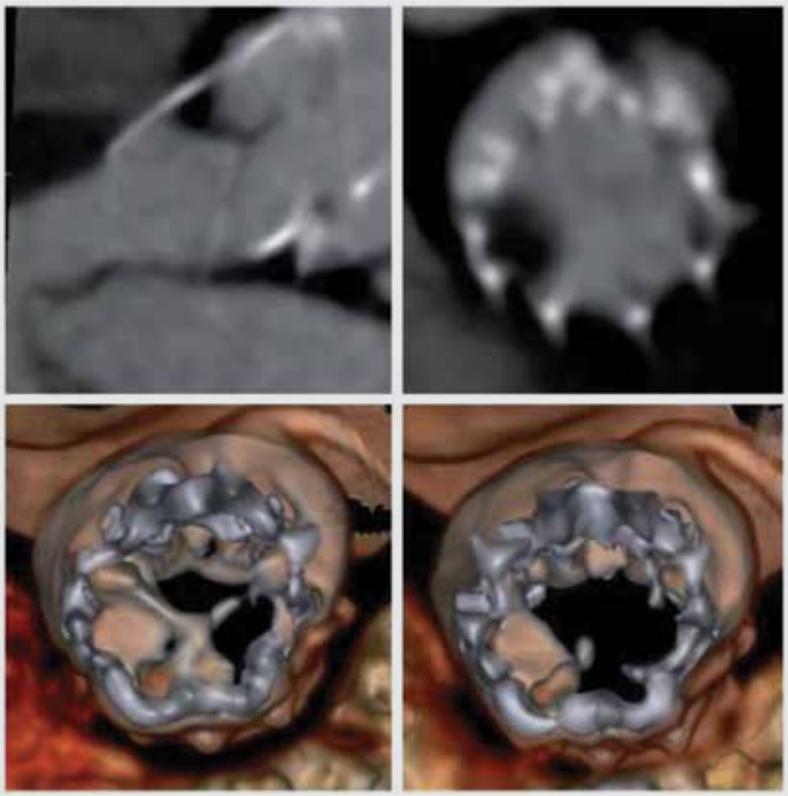

FIGURE 5. Portico valve with thick layer of hypo-attenuated leaflet thickening causing a severe reduction in leaflet motion (hypo-attenuation affecting motion). Top left panel: long axis multiplanar reconstruction in diastole; top right panel: axial multiplanar reconstruction diastole; Bottom left: diastolic volume rendering; bottom right: systolic volume rendering. Reproduced with permission from Sondergaard *et al.*[37]

nja potrebne su kako bi se otkrila uzročno-posljedična povezanost s HALT-om i HAM-om i ustalila personalizirana antikoagulantna terapija.[41]

Hibridno oslikavanje ili fuzijske slikovne metode

Prema trenutačno objavljenoj literaturi, uporaba fuzijskih slikovnih metoda općenito je u znatnom porastu i znanstvenim istraživanjima, ali i u kliničkoj kardiologiji. Različite komponente oslikavanja mogle bi se okarakterizirati kao anatomsko, funkcijsko i biološko oslikavanje. CT koronarografija je dobar primjer anatomskog oslikavanja jer vizualizira koronarne arterije i potencijalne stenoze, dok ehokardiografija i CMR omogućuju i funkcijsko i anatomsko oslikavanje. Nuklearne metode oslikavanja omogućuju funkcijsku procjenu (postojanje ishemije), ali su također i jedine metode koje omogućuju biološko oslikavanje – npr. kod upale s ^{18}F-FDG. Fuzijske metode oslikavanja mogle bi činiti fuziju ili integraciju različitih slika koje su dobivene izolirano te su poslije spojene ili integrirane za procjenu kardiovaskularne patofiziologije. van Rosendael *i sur.*[42] opisali su integriranu uporabu CT-a i ehokardiografije za bolju procjenu težine mitralne regurgitacije u 73 bolesnika. Kada je efektivni regurgitacijski

the time-course of HALT and HAM and establish personalized anticoagulation treatment.[41]

Hybrid imaging or fusion imaging

The literature reports an increasing use of fusion imaging in research but also in clinical cardiology. The different components of imaging can be categorized as anatomical, functional, and biological imaging. Coronary computed tomography angiography is a good example of anatomical imaging: visualizing the coronary arteries and potential stenoses; echocardiography and CMR provide both functional and anatomical imaging. Nuclear imaging can offer functional imaging (ischaemia assessment) but is currently the only technique that provides biological imaging: e.g. inflammation assessment with ^{18}F-FDG. *Fusion imaging* could represent the fusion or integration of different images that were *acquired in isolation and then later on fused or integrated* for assessment of cardiovascular pathophysiology. For example, van Rosendael *et al.*[42] described the integrated use of CT and echocardiography for improved assessment of severity of mitral regurgitation in 73 patients. When the effective regurgitant orifice was assessed by direct planimetry from CT, and this orifice size was then integrated with the velocity of the regurgitant flow on echocardiography (**Figure 6**), the severity of mitral regurgitation

otvor bio procijenjen direktnom planimetrijom CT-a, mjere su prenesene i integrirane s brzinom regurgitacije izmjerenom ehokardiografijom (**slika 6**), a težina je mitralne regurgitacije umjesto značajne opisana kao neznačajne u 10 % bolesnika, a kod 14 % bolesnika neznačajna regurgitacija bila je definirana kao značajna. Fuzijska tehnika tako je promijenila procjenu kod ukupno 24 % bolesnika; prognostička važnost fuzijskih slikovnih metoda još čeka daljnje dokaze.

Većina autora navodi kao hibridne metode uglavnom PET i CT, ali i PET i CMR. Novi uređaji omogućuju direktnu fuziju slika, koje su dobivene simultano ili jedna za drugom u istoj seriji. Raznoliki su primjeri objavljeni tijekom 2017. godine. Singh *i sur.*[43] objavili su rad o integraciji oslikavanja morfologije koronarnih plakova i upale koristeći se PET-CT-om s ^{18}F-

was downgraded from severe to non-severe in 10% of patients and upgraded from non-severe to severe in 14% of patients. Thus the fusion of the two techniques altered severity assessment in 24% of patients; the prognostic value of this fusion imaging remains to be demonstrated.

The majority of the literature reports on hybrid imaging, mostly with PET and CT, but also with PET and CMR. These new machines permit *direct fusion of both images*, which are acquired simultaneously or sequentially (in the same session). Various examples were reported in 2017. Singh *et al.*[43] reported on integrated imaging of coronary plaque morphology and inflammation using PET-CT with ^{18}F-FDG: 55 patients underwent imaging before and after 12 weeks of statin (atorvastatin) use. The ^{18}F-FDG uptake (target-to-background ratio)

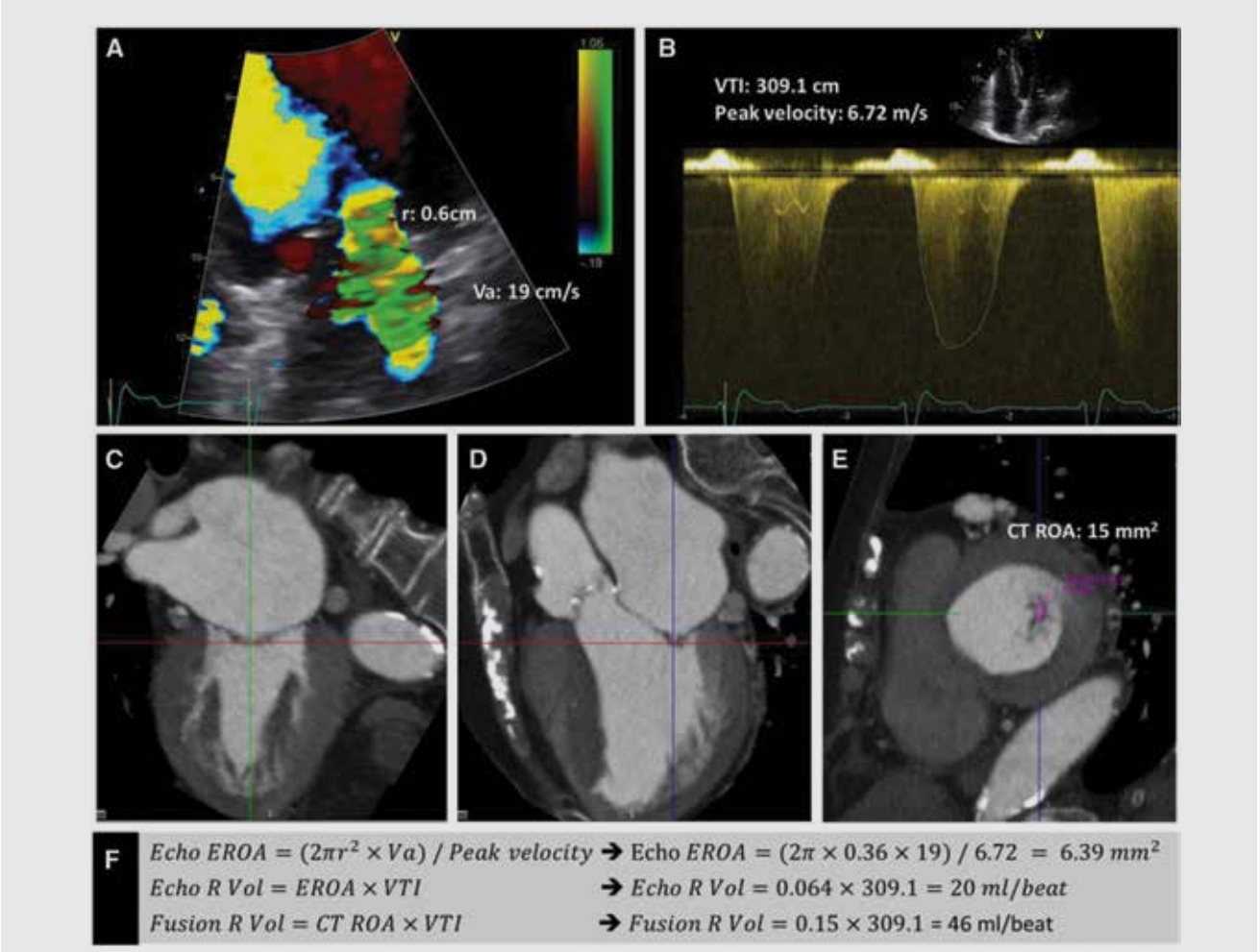

FIGURE 6. Integration of the Doppler echocardiography and computed tomography data to quantify mitral regurgitant volume. By echocardiography, the proximal isovelocity surface area method was used for the assessment of the effective regurgitant orifice area of the mitral regurgitation.(Panels *A*, *B*, and *F*) The velocity time integral of the magnetic resonance jet was assessed on the continuous wave Doppler images (Panel *B*). By aligning the multiplanar reformation planes on the multi-detector computed tomography data, a double oblique transverse plane parallel to the narrowest part of the mitral regurgitant orifice was reconstructed. The anatomical mitral regurgitant orifice area was measured by planimetry at this level (Panels *C–E*). The echocardiography and integrated regurgitant volume of magnetic resonance were assessed by multiplying the echocardiographic effective regurgitant orifice area and the multi-detector computed tomography derived mitral regurgitant orifice area with the velocity time integral, respectively (Panel *F*). Reproduced with permission from van Rosendael *et al.*[42]

VTI, velocity time integral; CT, computed tomography; ROA, regurgitant orifice area; RVol, regurgitant volume; EROA, effective regurgitant orifice area.

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FDG-om: 55 bolesnika sudjelovalo je prije i nakon 12 tjedana terapije statinima (atorvastatin). Apsorpcija ^{18}F-FGD (ciljano na pozadinski omjer) je bila procjenjivana u lijevoj koronarnoj arteriji te je bilo mnogo više apsorpcije kod nekalcificiranih ili djelomično kalcificiranih lezija verificiranih CCTA-om (koje su smatrane visokorizičnim lezijama) u usporedbi s kalcificiranim lezijama (ciljano na pozadinski omjer 1,95 ± 0,43 prema 1,67 ± 0,32, P= 0,04). Nakon 12 tjedana terapije statinima, primijećeno je znatno smanjenje apsorpcije ^{18}F-FDG-a kod visokorizičnih lezija.

Primjenom PET-CMR-a[44] evaluirani su bolesnici sa suspektnom sarkoidozom (n = 25). Aktivna je sarkoidoza bila definirana kao veća apsorpcija ^{18}F-FDG-a u područjima s odgodom pojačanja kontrasta na CMR-u (prisutno u 8 bolesnika); u ostalih drugi nalaz nije upućivao na sarkoidozu. Ovakav bi pristup mogao omogućiti identifikaciju bolesnika s aktivnom sarkoidozom i omogućiti selektivnu terapiju.

PET-CT omogućuje preciznu detekciju endokarditisa u bolesnika koji su bili podvrgnuti transkateterskoj ugradnji aortne valvule[45]. Kompjutorizirana tomografija omogućuje prikaz zadebljanja listića (kao markera za trombozu), a ^{18}F-FDG indicira aktivnu upalu. Ovakav pristup s oslikavanjem superioran je nad rutinskom procjenom endokarditisa prema Dukeovim kriterijima.

U studiji EVINCI bilo je uključeno ukupno 14 centara iz devet europskih zemalja s ukupno 252 bolesnika sa stabilnom anginom i osrednjom vjerojatnošću CAD-a[46]. Bolesnicima je bilo učinjeno SPECT ili PET perfuzijsko oslikavanje i CCTA te su dobiveni nalazi integrirani. Ove neinvazivne tehnike oslikavanja bile su potom uspoređene s invazivnom koronarnom angiografijom kombiniranom s FFR (za detekciju hemodinamski značajnih stenoza). Hibridno je oslikavanje isključilo funkcionalno signifikantnu CAD u 41 % bolesnika, što je negativna prediktivna vrijednost od 88 %, utvrdilo signifikantnu bolest u 24 % bolesnika, što je pozitivna prediktivna vrijednost od 87 %. Zaključno, kako bi hibridno oslikavanje dobilo važniju ulogu u dijagnostici značajne CAD sa svrhom izbjegavanja nepotrebnih invazivnih koronarnih intervencija, potrebno je više istraživanja.

was assessed in the left main coronary artery, which was significantly higher in non-calcified or partially calcified lesions on CCTA (considered high-risk) as compared to calcified lesions (target-to-background ratios 1.95 ± 0.43 vs. 1.67 ± 0.32, P = 0.04). After 12 weeks of statin use, there was a significant reduction in ^{18}F-FDG uptake in the high-risk lesions.

Patients (n = 25) with possible sarcoidosis were evaluated with PET-CMR;[44] active sarcoidosis was defined as having increased ^{18}F-FDG uptake in areas with delayed contrast-enhancement on CMR (present in eight patients); all other patients did not show active sarcoidosis. This approach may enable identification of patients with active sarcoidosis and permit selective treatment.

Positron emission tomography–computed tomography enabled accurate detection of endocarditis in patients who underwent transcatheter aortic valve replacement.[45] Computed tomography demonstrated leaflet thickening (as marker of thrombosis), whereas ^{18}F-FDG indicated active inflammation; the imaging approach was superior over routine assessment of endocarditis (according to the modified Duke criteria).

In the EValuation of INtegrated Cardiac Imaging for the Detection and Characterization of Ischaemic Heart Disease (EVINCI) study, 14 centres from nine European countries included 252 patients with stable angina and intermediate pre-test likelihood of CAD.[46] The patients underwent SPECT or PET perfusion imaging and CCTA, and these images were fused on a dedicated workstation. These non-invasive imaging data were compared with quantitative invasive coronary angiography with assessment of FFR (to detect haemodynamically significant stenosis). Hybrid imaging excluded functionally significant CAD in 41% of patients, which provided a negative predictive value of 88%, and included in significant disease in 24% of patients, which yielded a positive predictive value of 87%. To establish the role of hybrid imaging in the detection of significant CAD, additional studies are needed focusing on the influence of this imaging modality on the downstream of patients (avoiding unnecessary invasive coronary angiography and interventions).

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