

# Cardiac magnetic resonance tomography : clinical data on the feasibility and validity in old and very old patients

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**UNIVERSITY OF SPLIT  
SCHOOL OF MEDICINE**

**Laura Hartnik**

**CARDIAC MAGNETIC RESONANCE TOMOGRAPHY – CLINICAL DATA ON  
THE FEASIBILITY AND VALIDITY IN OLD AND VERY OLD PATIENTS**

**Diploma thesis**

**Academic year:**

**2021/2022**

**Mentor:**

**Prof. Johannes Brachmann, MD, PhD**

**Coburg, July 2022**

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## **LIST OF ABBREVIATIONS**

ACS – Acute coronary syndrome

AF – Atrial fibrillation

AP – Angina pectoris

AV-node – Atrioventricular node

CAD – Coronary artery disease

cMRI – Cardiac magnetic resonance imaging

CVD – Cardiovascular diseases

ECG – Echocardiogram

EGE – Early gadolinium enhancement

ICD – Implantable cardioverter defibrillator

LA – Left atrium

LAX – Longitudinal axis

LGE – Late gadolinium enhancement

LV-block – Left ventricle block

LVOT – Left ventricular outflow tract

MI – Myocardial Infarction

MRI – Magnetic resonance imaging

NSTEMI – Non-ST-elevation myocardial infarction

PV – Pulmonary vein

PVI – Atrial ablation therapy

SAX – Short axis views

STEMI – ST-elevation myocardial infarction

TI – Time inversion

U.S. – United States of America

VAD – Ventricular assist device



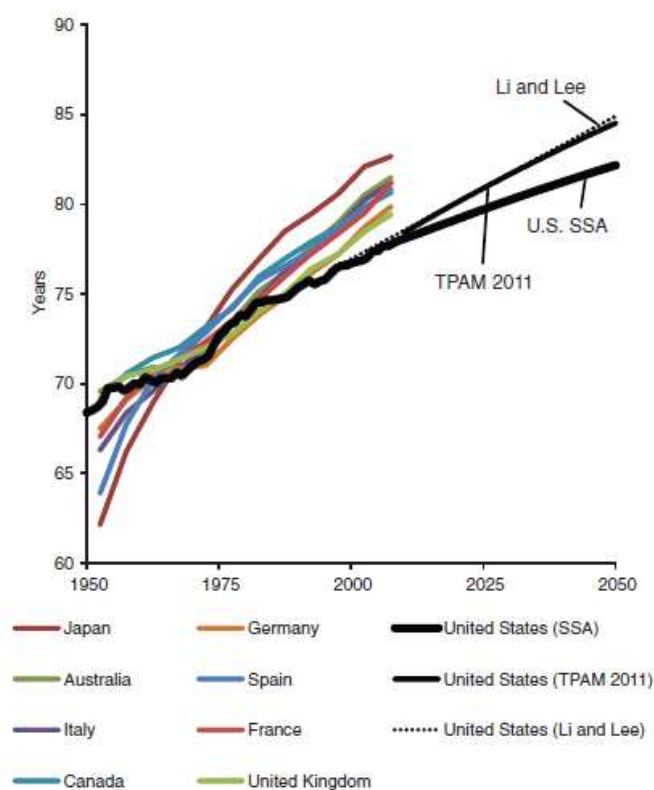
## **1. INTRODUCTION**

## 1.1. Demographic Change

In future, we are experiencing a demographic change as the population is getting older worldwide. This happens at different rates depending on the country and region and even between regions in the same country. In developed countries the effects of the change are more advanced than in developing countries. The explanation for the demographic change lies in two demographic trends (1,2).

### 1.1.1. Higher Life Expectancy

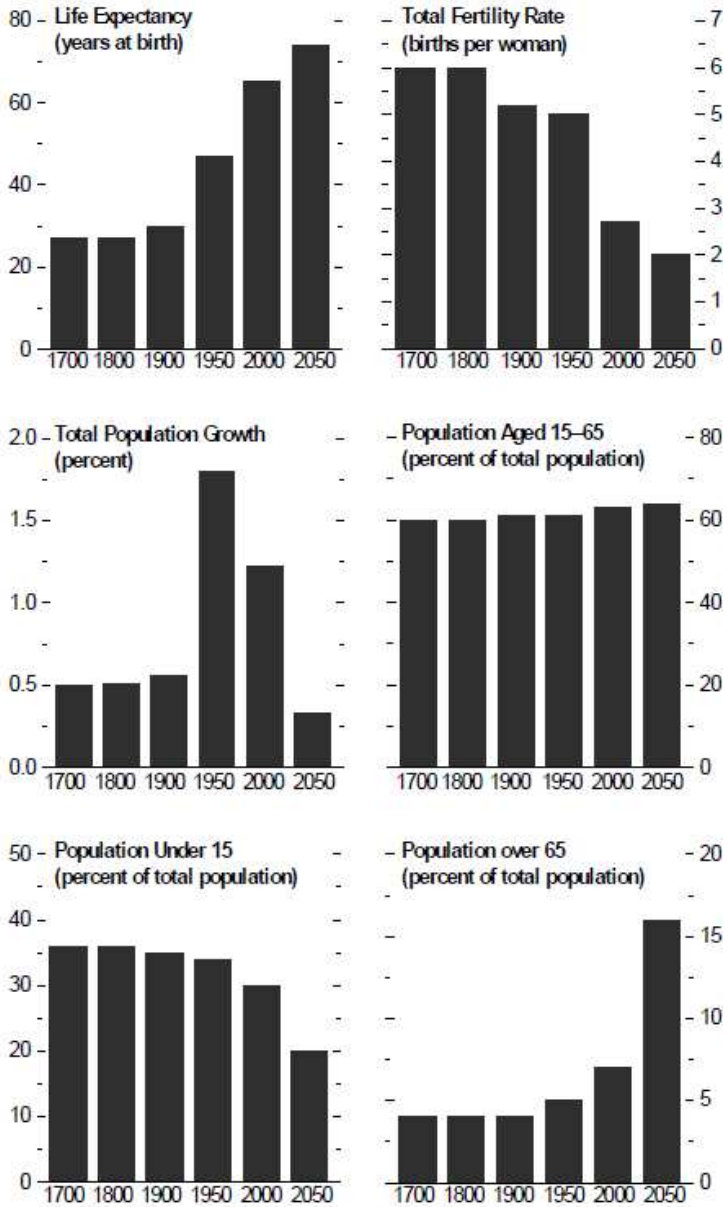
Due to improved medical knowledge in treating diseases and consequently improved public health and survival especially in children and older people, as well as a general better nutrition, people have a higher life expectancy. In Europe it has increased by 10 years in the last 50 years for both sexes. In Germany, for example, life expectancy gained three months per year in the last 150 years up to an estimated life expectancy of 85 years for men and 89.2 years for women in 2060. In the United States of America, the average life expectancy was 67 years



**Figure 1. Life expectancy trends in the U.S., Australia, Canada, France, Germany, Italy, Japan, Spain, and the United Kingdom**

Source: Institute of Medicine (US) Committee on the Long-Run Macroeconomic Effects of the Aging U.S. Population. *Aging and the Macroeconomy: Long-Term Implications of an Older Population*. Washington (DC): National Academies Press (US); 2012. p. 33

for males and 73 years for females in the last century whereas nowadays it is 76 years for men and 81 years for women. These trends can be seen in Figure 1 and Figure 2 describing the global as well as the change in some of the western countries (1–5).

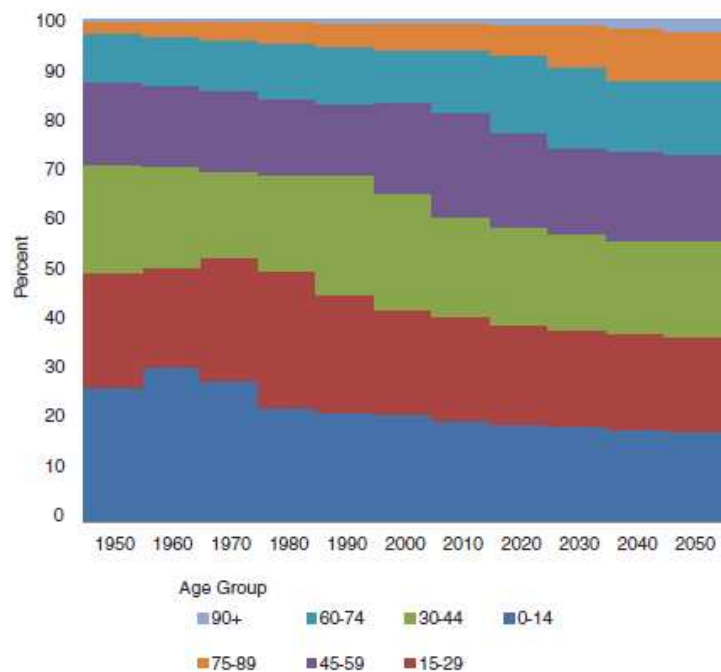


**Figure 2. Global demographic transition between 1700 and 2050**

Source: Batini N, Callen T, McKibbin WJ. The global impact of demographic change. SSRN Electronic Journal. 2006. doi:10.2139/ssrn.888154. p. 5

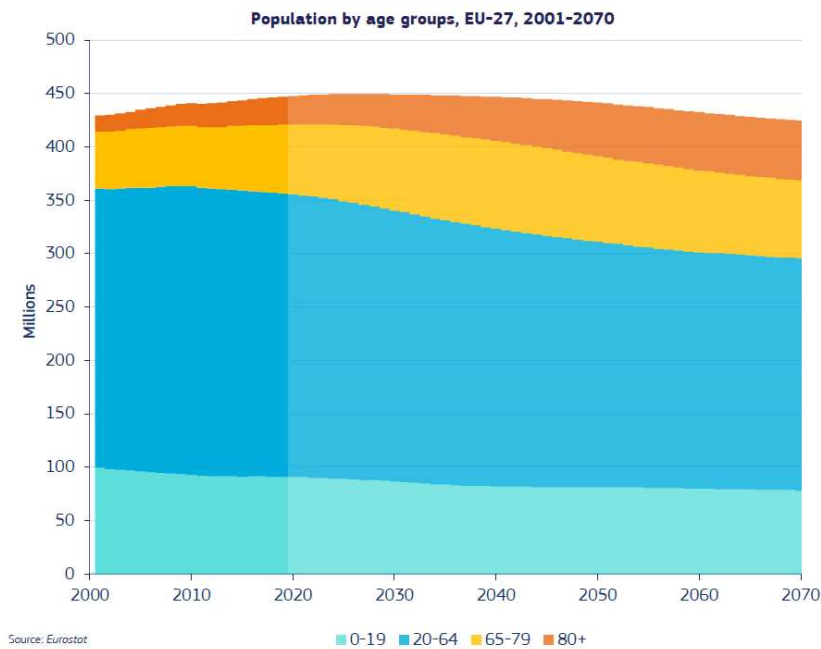
### 1.1.2. Lower Birth Rates

The second reason for demographic change is decreasing birth rates due to more women deciding to have fewer or no children, to have kids at a later stage of life and changes in family concepts. In the sixties of the last century, we experienced a baby boom with a fertility rate counting 3.7 births per women. In the last decades it declined to 2.1 births per women in the U.S. and 1.4 in Germany. Therefore, people in Europe with over 65 years of age are gaining ground. Right now, the population age 65 and older account for roughly 20% of the whole population. In Germany this corresponds to the same percentage that the population age 20 and below represents. By 2070 this percentage is estimated to be 30%, in Germany even slightly earlier and up to 34% by 2060. The part of the population age 80 and older is predicted to at least double between 2019 and 2070. Similarly, in the US people over 65 years of age will outgrow people of 20-64 years of age with an increase by 80 percent (1, 3, 4). The population distribution by age is shown in Figure 3 and 4.



**Figure 3. Population distribution by age in the U.S. between 1950 and 2050**

Source: Institute of Medicine (US) Committee on the Long-Run Macroeconomic Effects of the Aging U.S. Population. *Aging and the Macroeconomy: Long-Term Implications of an Older Population*. Washington (DC): National Academies Press (US); 2012. p. 42



**Figure 4. Population distribution by age in Europe between 2000 and 2070**

Source: European commission. European Commission Report on the Impact of Demographic Change. 2020 June 18 [cited 2022 May 20]. p. 10 Available from: [https://ec.europa.eu/info/sites/default/files/demography\\_report\\_2020\\_n.pdf](https://ec.europa.eu/info/sites/default/files/demography_report_2020_n.pdf)

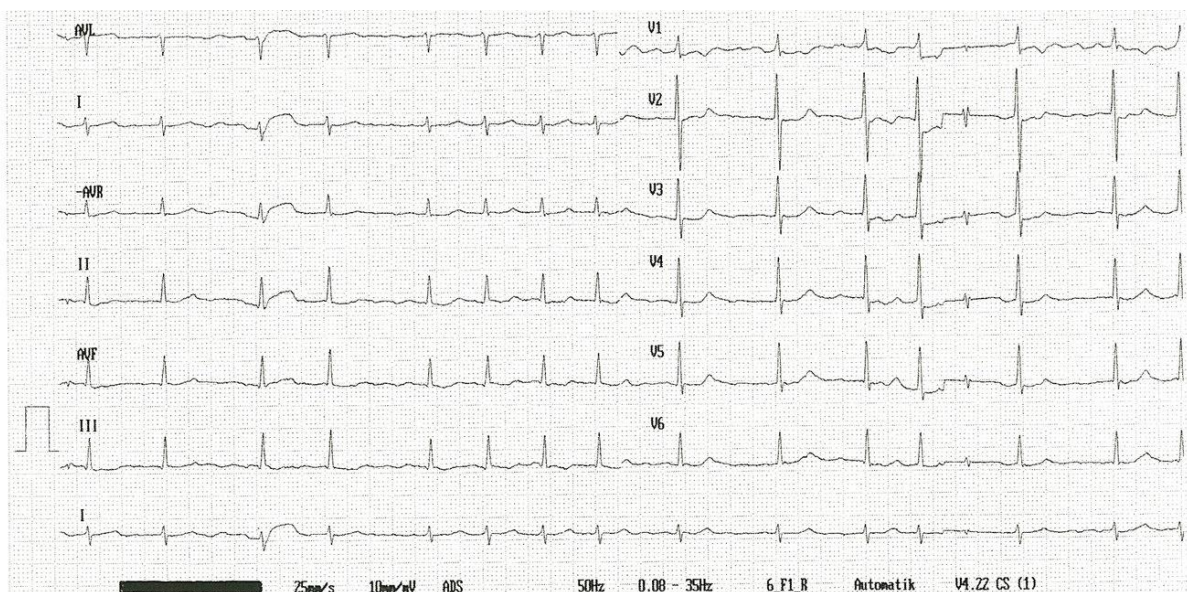
## 1.2. Cardiovascular Diseases in Older People

Associated with older age is an increase in cardiovascular events, as in this phase of life biological changes predispose to the development and progression of cardiovascular disease (CVD) (6,7). The most common CVD among the older population are atrial fibrillation (AF), myocardial infarction (MI) and coronary artery disease (CAD).

### 1.2.1. Atrial Fibrillation (AF)

The most common cardiac arrhythmia is AF (8–13). About 1-2% of the general population is affected and the estimated lifetime risk is between 22 and 26 percent (8,12). The average age of patients today is between 75 and 85 years (10). AF is a supraventricular arrhythmia with until today not exactly defined cause. There are several risk factors identified, such as different heart diseases as well as endocrinologic disorders. The clinical picture is diverse. Several patients are asymptomatic, but many present themselves with palpitations, lightheadedness, and shortness of breath. The pulse is always irregular. AF leads to atrial dysfunction which can result in the stasis of blood and a subsequent clot formation (14). The diagnosis can be established by electrocardiogram (ECG) recordings where you can see the lack

of a p wave and irregular QRS complexes as seen in Figure 5 (8,14). Most relevant complications are embolic stroke and worsening heart failure. These are contributing factors to the associated increase in mortality and morbidity (8,10,12,13). For treatment several approaches are possible. Patients receive anticoagulation therapy, according to a risk stratification score (CHA<sub>2</sub>DS<sub>2</sub>VASc-Score) to prevent secondary outcomes like stroke or systemic embolism (9,10,15). One of the ways to treat AF is by rate control using medications affecting the atrioventricular node (AV-node) like  $\beta$ -adrenergic receptor blockers, non-dihydropyridine calcium channel blockers and digitalis glycosides. The second way to treat atrial fibrillation is by rhythm control, i.e., conversion of the heart rhythm to sinus rhythm. This is achieved by either antiarrhythmic drugs, by using electrical cardioversion (8,15) or by atrial ablation of the site where the ectopic impulses are coming from, most often from the area around the pulmonary veins (80-94%), but also from various other spots within the left atrium. It is an efficient and secure strategy to control the rhythm in patients that do not experience an improvement or do not want to take medical therapy (10,16,17).



**Figure 5. ECG recording of arrhythmia absoluta in atrial fibrillation**

Source: Amboss – Knowledge for medical students and physicians (27.05.2022)

<https://next.amboss.com/de/article/GS0Baf?q=vorhofflimmern&m=em0xeg#Ze8f59c6fdb873abb8b66b786d0397266>

### **1.2.2. Coronary Artery Disease**

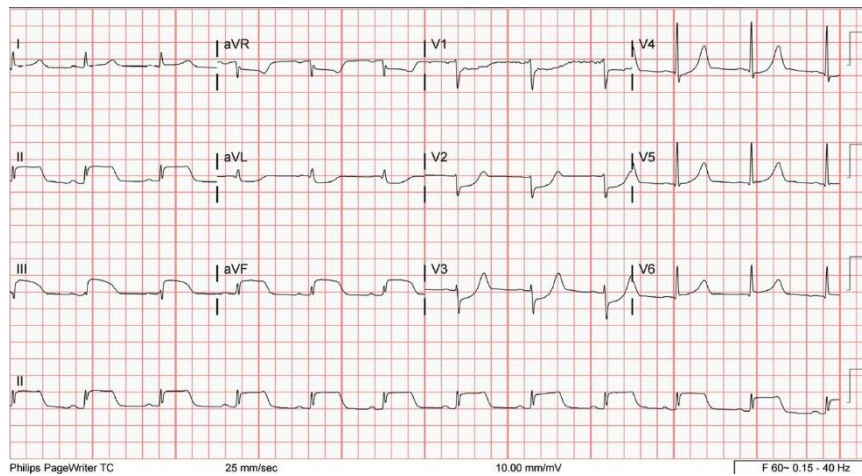
Coronary artery disease (CAD) is a disorder most often caused by atherosclerotic obstructing plaques in the coronary arteries and the resulting reduced blood supply to the cardiac muscle, the myocardium, leading to a mismatch between myocardial oxygen supply and demand. Other, more rare causes are coronary vasospasms and very seldom emboli and congenital abnormalities. The leading clinical feature is angina pectoris, an acute retrosternal chest pain, usually radiating to the jaw and arm. Other symptoms like dyspnea, dizziness, anxiety, nausea, vomiting and diaphoresis can also occur. CAD can be divided into stable CAD and severe myocardial ischemia. Stable CAD is either asymptomatic or consists of stable angina which appears only during exertion, mental stress, or exposure to low temperature and usually stops after about 20 minutes of rest or application of nitroglycerin. Severe myocardial ischemia can advance to acute coronary syndrome (ACS) up to myocardial infarction (MI). Diagnosis of stable CAD is established by anamnesis with corresponding clinical findings, cardiac imaging and different stress testing methods using ECG, echocardiography, scintigraphy, magnetic resonance imaging (MRI) and finally coronary catheterization. Its treatment comprises the prevention of progression of atherosclerosis (lifestyle changes, sports, elimination and/or improvement of risk factors), antianginal- and antiplatelet medication, as well as revascularization by cardiac catheterization in advanced disease or coronary bypass surgery. Typical medications for a person with CAD are nitroglycerine, acetylsalicylate acid, statins,  $\beta$ -adrenergic blocker, renin-angiotensin-aldosterone-system inhibitors (15,18,19).

### **1.2.3. Myocardial Infarction (MI)**

MI is an acute necrosis of myocardial tissue by an ischemic insult due to a ruptured plaque or an occluded artery, that creates a mismatch in oxygen supply and demand. Its clinical manifestation is ACS characterized by acute chest pain and can have altered ECG and pathological troponin findings. The extend of the presentation is decisive for the treatment. MI findings in ECG are divided into ST-elevation MI (STEMI, seen in Figure 6) and non-ST-elevation MI (NSTEMI), with STEMI being the more severe form. Clinical diagnosis is confirmed by cardiac catheterization, which is also used to revascularize the affected part of the artery. Another part of the treatment is secondary prevention, usually with dual antiplatelet therapy,  $\beta$ -adrenergic blocker and/or renin-angiotensin-aldosterone-system antagonists, statins and measurements to reduce modifiable risk factors (15,18,20,21). Cardiovascular disease is the main cause of death in many European countries. Therefore, for primary and secondary



prevention, diagnostics that are as accurate and gentle as possible are necessary. This applies particularly to vulnerable cohorts, such as old and very old people.



**Figure 6. Inferoposterior ST-elevation myocardial infarction**

Source: Amboss – Knowledge for medical students and physicians (25.05.2022)  
<https://next.amboss.com/us/article/Yq0nCS?m=FRbgKt>

### 1.3. Diagnostic Challenges in Older Patients

Age does not only affect the cardiovascular system, but leads to other physiological changes as well, which can alter the function of a lot of systems. Elderly people mostly have not only one disease, but several comorbid diseases up to geriatric syndromes (e.g., frailty, disability, cognitive decline, and sarcopenia). Because of these multiple comorbidities patients are prescribed several medications, predisposing to drug-drug interactions and due to altered function of excretory organs different drug action itself. These circumstances can make the interpretation of traditional CVD assessments very challenging (5). The same counts for diagnostic biomarkers and imaging regarding CVD. We have a lot of data on how to interpret them in younger people, but very few that also include the differences in the elderly and very elderly population. The normative ranges for biomarkers are an example: an age-based spectrum is needed to be able to know when to best think about the disease. Moreover, common diseases of the elderly, such as Parkinson, arrhythmias leading to pacemaker implantation, kyphoscoliosis, chronic lung diseases, dementia, and advanced chronic kidney disease, have an impact on imaging quality or can be a contraindication for imaging for itself. Especially in stress-testing older individuals are often not suitable for ergometric tests due to musculoskeletal problems and poor fitness levels. On top of that, certain medications that are used in diagnostic procedures can have an impact on preexisting conditions or provoke new

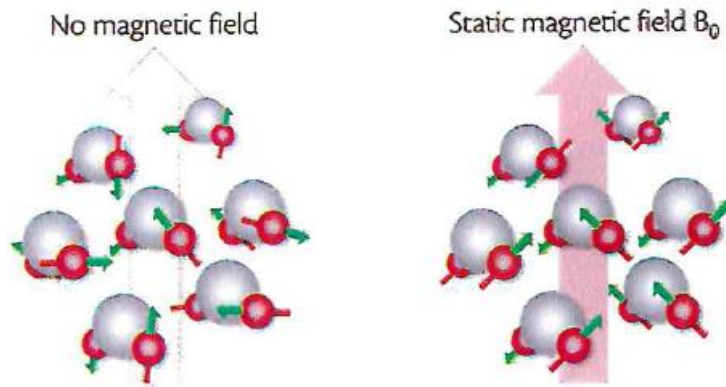


conditions itself, such as dobutamine (used in stress-testing) which can induce or deteriorate arrhythmias or contrast agents (imaging) that can affect the kidney function (22). This study focuses on the feasibility of cardiac MRI (cMRI) in elderly and very elderly patients and wants to determine if this patient population can benefit from MRI diagnostic despite these diagnostic challenges.

## **1.4. Cardiac Magnetic Resonance Imaging (MRI)**

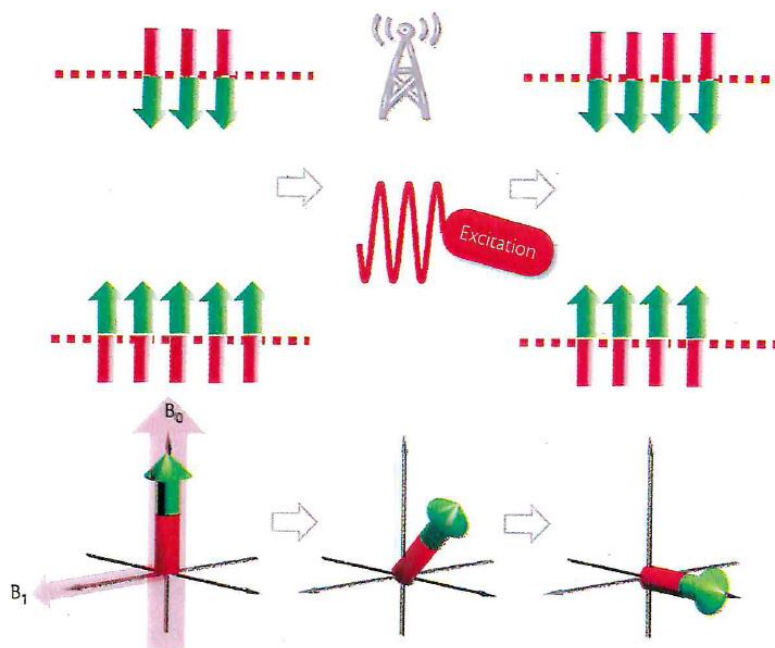
### **1.4.1. General Principles of MRI**

MRI is a tomographic imaging modality using electromagnetic fields and radio waves to create a picture of the scanned body structures. The image is generated by using the magnetic properties of hydrogen protons established by an intrinsic angular momentum, i.e., a spin (magnetic moment). When these protons are exposed to a strong, static external magnetic field ( $B_0$ ), e.g., an MRI, in a specific plane (plane  $Z$ ), they align in themselves in a parallel or antiparallel orientation, as seen in figure 7. If a radiofrequency field ( $B_1$ ) is turned on, with a strength weaker than that of the static magnetic field, protons will transit into a different energy state which then causes the rotation of net magnetization into a plane orthogonal to the static magnetic field  $B_0$ . This is called excitation and is illustrated in Figure 8. After the radiofrequency field is turned off protons will return to the initial plane of  $B_0$ . This process is called relaxation. Through the process of relaxation protons loose energy to their surroundings. A special coil detects this energy or signal and transforms it into an image. The time needed for relaxation depends on the tissue type, as different amount of protons are in different tissues and within different textures of one tissue, thus the generation of contrast in an MRI (23,24).



**Figure 7.** Here seen are the two protons of the water molecule (red spheres). Each proton possesses a magnetic moment. Without an external magnetic field, the orientation is random (left). When a static magnetic field ( $B_0$ ) they align in a parallel or anti-parallel orientation relative to  $B_0$  (right).

Source: Lombardi M, Plein S, Petersen S, Bucciarelli-Ducci C, Valsangiacomo Buechel ER, Basso C et al. The EACVI Textbook of Cardiovascular Magnetic Resonance. New York: Oxford University Press; 2018. p. 7.



**Figure 8.** Turning on a radiofrequency field ( $B_1$ ) causes the protons to transit into a different energy state and rotate the net magnetization into a plane orthogonal to  $B_0$ .

Source: Lombardi M, Plein S, Petersen S, Bucciarelli-Ducci C, Valsangiacomo Buechel ER, Basso C et al. The EACVI Textbook of Cardiovascular Magnetic Resonance. New York: Oxford University Press; 2018. p. 8.

As MRI acts based on magnetic fields it has the potential to interact with ferromagnetic metals. These can be found in several implants and medical devices used in medicine. Among these we can divide between active implants, such as cardiac pacemakers, implantable cardioverter-defibrillators (ICD), implantable loop recorder, ventricular assist devices (VAD), cochlear implants and implanted neurostimulators and passive implants such as heart valves, stents, orthopedic implants, and dental implants. There can be force and torque effects due to ferromagnetic objects being attracted to the strong magnet field of the MRI. Moreover, alteration or destruction of magnet functions of implants such as cochlear implants or dental implants can occur. The correct function of pacemakers and ICDs can be affected, as well, causing a potential danger to the patient. Finally, the radiofrequency field can induce increased heating of tissues surrounding these implants and devices (23,25). VAD and neurostimulators are not compatible with MRI whereas there are no absolute contraindications for all other implants and devices if certain conditions (often described by the manufacturer) to reduce the are met to reduce the risk of interaction (25,26).

#### **1.4.2. Role of MRI in Cardiology**

Cardiac MRI has become a standard diagnostic tool, as it yields high quality images of the whole cardiovascular system. It has improved over the last years in temporal resolution, spatial resolution, motion-, and other artifact reduction and delivers precise information about myocardial tissue function and allows tissue characterization. Nowadays we can use cardiac MRI to measure heart morphology, heart function, myocardial perfusion, infarct size, transmural extend of myocardial necrosis, microvascular obstruction, myocardial edema, and hemorrhage, which together gives us a better picture of the hearts viability and extend of possible diseases. Gadolinium-based contrast agents are of great importance to cardiac MRI. Gadolinium acts by shortening the relaxation time of protons in its vicinity, thus enhancing the contrast of tissues (23). It is an extracellular medium and has shown to be safe and useful in MRI diagnostics. For example, in myocardial scars there is an expansion of the extracellular space, thus more uptake (Wash-In) and slower elimination (Wash-Out) of gadolinium opposed to normal myocardial tissue. Several minutes (10-20 minutes) after intravenous administration of gadolinium, the contrast agent is washed in the myocardium and scars appear bright (= enhanced signal) on MRI. This is called late gadolinium enhancement (LGE), which allows to detect myocardial scars and therefore improve the assessment of myocardial viability (27). Another important feature about LGE imaging is, that it has a great intra- and inter-observer agreement and is highly reproducible (28,29). With LGE it is also able to detect subendocardial

infarction which may have been previously unrecognized, infiltrative cardiomyopathies (e.g., cardiac amyloidosis, cardiac sarcoidosis) and scar tissue which is important to estimate the patient's prognosis and predispositions to possible complications. Cardiac MRI seems to be at least equal if not superior to other diagnostic techniques at present (22,30–33). As with many other diagnostic and interventional procedures in cardiology, our assessment of the usefulness and feasibility of cMRI is based on evidence derived primarily from findings in younger patients. Data from old or very old people are only available in small amounts.

## **2. OBJECTIVES AND HYPOTHESIS**

## **2.1. Aims**

The objective of this study was to determine if cardiac MRI is a safe diagnostic tool regarding cardiac disease in everyday clinical practice in old and very old people. Additionally, this study aims to evaluate the validity of the diagnostic data obtained in the cardiac MRI.

## **2.2. Hypothesis**

Cardiac MRI is a safe and effective diagnostic tool in elderly and very elderly patients.

### **3. MATERIALS AND METHODS**

### 3.1. Study Project

This retrospective study took place at the Department for Cardiology and Angiology at Regiomed Hospital Coburg in Germany. The data analyzed in this study had been collected between February 3<sup>rd</sup>, 2014 and November 29<sup>th</sup>, 2021. The study was ethically approved by the Institutional Review Board of the Regiomed Medical School on 18 March 2022. All data and rights of patients were protected in accordance with the World Medical Association Helsinki declaration of 2013. A total of 1153 patients (567 males, 586 females, mean age 82±2.9 years, range 80-100 years) who received a cardiac MRI (3.0 T Verio, Siemens, Erlangen, Germany) as part of their inpatient treatment were included in the final analysis. Most of the patients were between 80 and 89 years old (1118; 97%), fewer patients were over 90 years (35; 3%). The result of magnetic resonance imaging had already been assessed by trained and experienced cardiologists of the Regiomed Hospital Coburg. Our analysis focused on the indication of the MRI, whether the MRI was aborted by the patient and if the MRI images had had a sufficient quality to be properly evaluated regarding the medical question.

Inclusion criteria: All patients over 80 years receiving a cardiac MRI as part of their inpatient treatment at the Regiomed Hospital Coburg were included.

Exclusion criteria: Patients below the age of 80 by the time of the MRI were not included, as well as all patients over 80 years that were documented to have had an MRI, but whose data could not be found in the hospital data base due to technical difficulties or that had no according report in the system.



**Figure 9. MRI Verio 3.0 T Siemens, Erlangen, Germany**



### **3.2. Used Cardiac MRI Protocols**

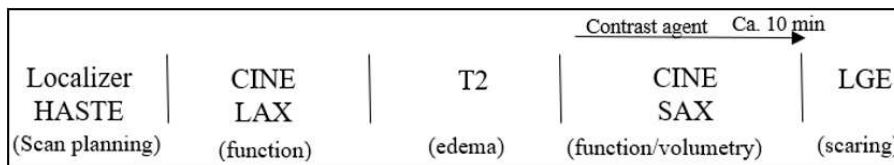
In clinical practice, different cardiac MRI protocols are used for different diagnostic question. In our study, most MRI scans aimed to detect myocardial ischemia by stress testing using adenosine or dobutamine (27.4%), viability testing after myocardial infarction (26.4%), imaging before and after left atrial ablation for AF (19.8%) and myocarditis (18.6%). The remaining scans (7.8%) were related to less common indications such as tumors, thrombi, or systemic diseases. All cardiac MRIs took between five to 80 minutes of time (mean  $40 \pm 10.46$  minutes).

#### **3.2.1. Standard Sequences**

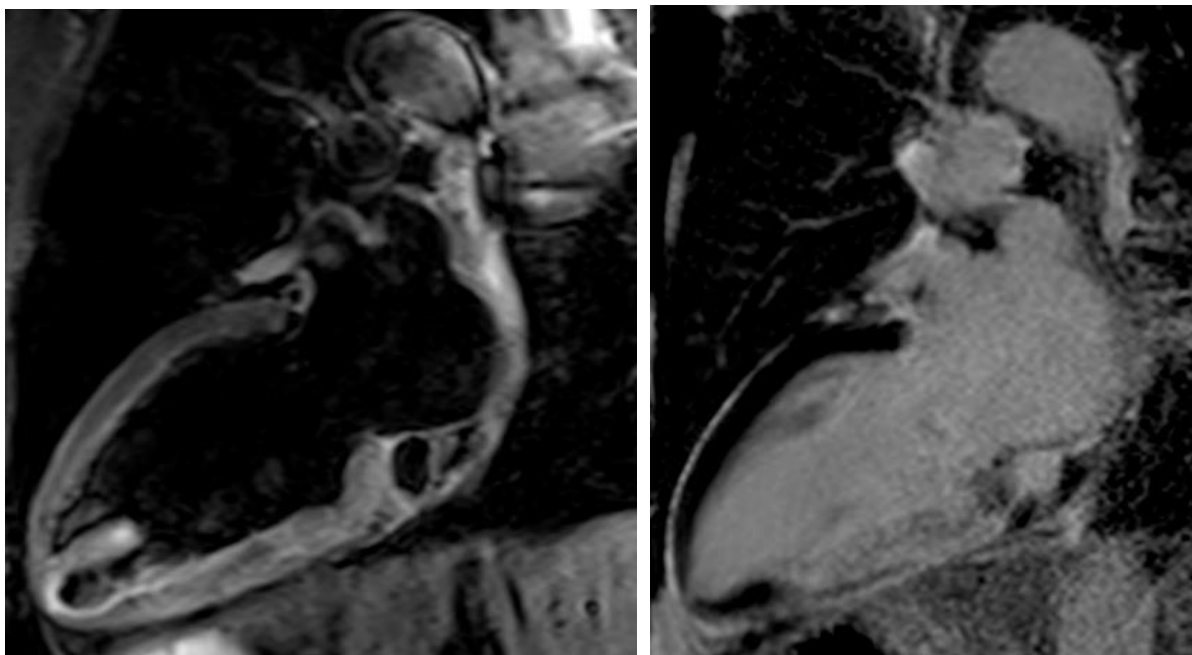
Every cardiac MRI starts with certain standard scans, irrespective of the clinical question. First come the *Localizer* images in axial, coronal, and sagittal planes, which are used to plan the axis of heart. Second is the *HASTE*, which is in axial stack, depicting an overview of the whole thorax. Third, after running a frequency scout to detect any artifacts and changing the settings where required, come the *CINE* sequences, which are moved pictures to assess the heart function. They are routinely scanned in longitudinal axis (LAX), i.e., in a four-chamber view (both atria and both ventricles), a two-chamber view (left atrium and ventricle) and a three-chamber view (left atrium, left ventricle and aorta), and in multiple short axis views (SAX). The latter are usually done at later stages during the scan depending on the protocol and to reduce total scan time. The subsequent sequences differ depending on the diagnostic purpose of the scan taken.

### 3.2.2. Viability Assessment

With cardiac MRI we can look for acute and chronic viability of the heart muscle. Therefore, we use acute viability testing (e.g., after acute MI) and chronic viability testing (e.g., in coronary syndrome). We are always starting with our above-mentioned standard scans. In the acute setting we run a *T2* sequence in four-chamber-, two-chamber-, and three chamber view. In this sequence we can see any signs of myocardial edema, suggesting acute myocardial damage. This is followed by an injection of contrast agent (Clariscan, GE Healthcare GmbH, 0,3 bis 0,4 mmol/kg). Approximately 10 minutes after having administered the contrast agent, we can start with the late gadolinium enhancement (*LGE*) scans. These images comprise again four-, three-, and two-chamber views as well as three SAX (basal, midventricular and apical slice). Signal enhancement in these sequences shows us myocardial scars. We conclude the *LGE* measurement with performing a *3D-LGE*-scan of the left ventricle, which often improves our judgement concerning extent, severity, and localization of the scars. In the chronic viability setting we use the same scans as in the acute setting without need for *T2* sequences, because we don't expect edema in these patients.



**Figure 10. Viability: MRI Protocol**



**Figure 11. Examples of viability assessment MRI pictures. Left: *T2* weighted (after an inferior wall infarction); Right: *LGE*.**

### 3.2.3. Stress Testing

Cardiac stress testing is used to detect myocardial ischemia in early stages. With cardiac MRI, we usually use the drug adenosine for stress induction. In case of contraindications for adenosine (e.g., bronchial asthma or higher atrioventricular block), we can use dobutamine. After having done the initial standard sequences, we additionally scan the left ventricular outflow tract (LVOT) and the aortic valve to check for severe aortic stenosis (contraindication for stress testing). In case of adenosine stress, we now start with the stress perfusion sequence. We therefore infuse the patient with adenosine according to a standard dosing scheme (140µg/kg/min) over six minutes and when the heart rate reaches the maximal point, we give a contrast agent and start a perfusion scan consisting of three SAX (basal, midventricular and apical parts of the heart), and then perform a *CINE* scan in four-chamber-, two-chamber- and three-chamber view. After the heart rate gets back to normal, we repeat the contrast agent infusion and perform the perfusion scan again, i.e., rest perfusion sequence. When using dobutamine stress, we infuse the patient with dobutamine according to a standard dosing scheme (dose is adjusted to age and intended heart rate:  $(220 - \text{age}) \times 0.85$ ) over several minutes, as long as it is needed to reach the target heart rate. During that time, we perform repeatedly *CINE* scans in four-chamber-, two-chamber- and three-chamber view and three SAX (basal, midventricular and apical parts of the heart). The last scans are for viability assessment (details see 3.2.2), where we are looking for scar tissue using *LGE*.

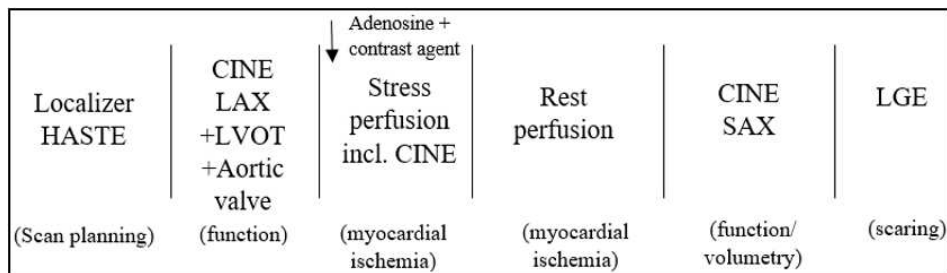


Figure 12. Stress testing: MRI protocol

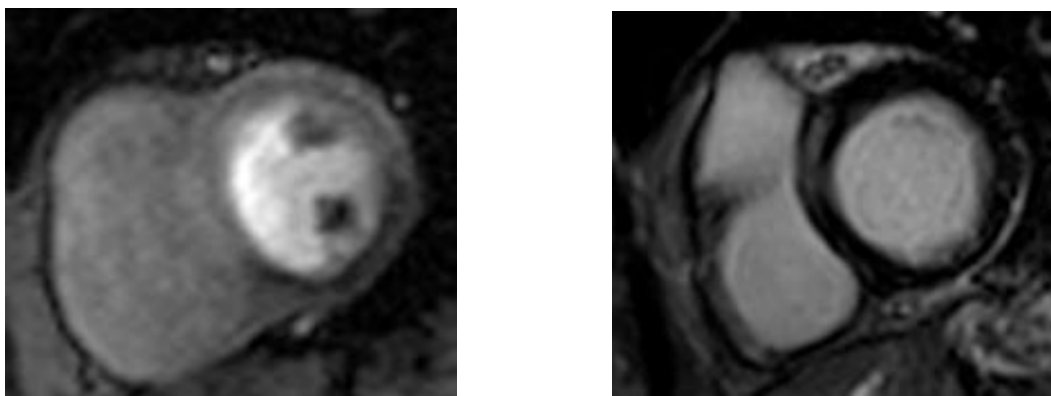


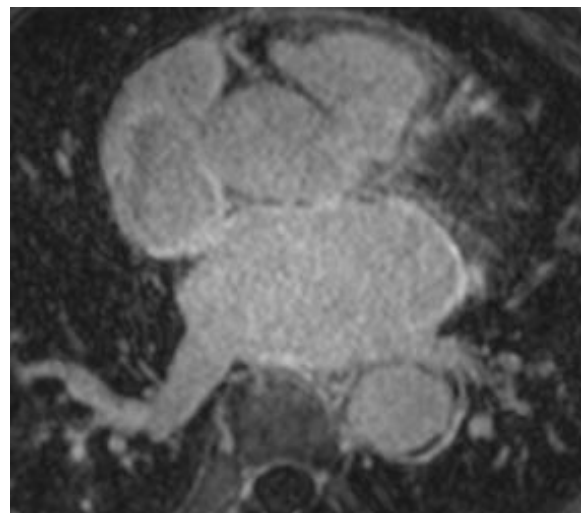
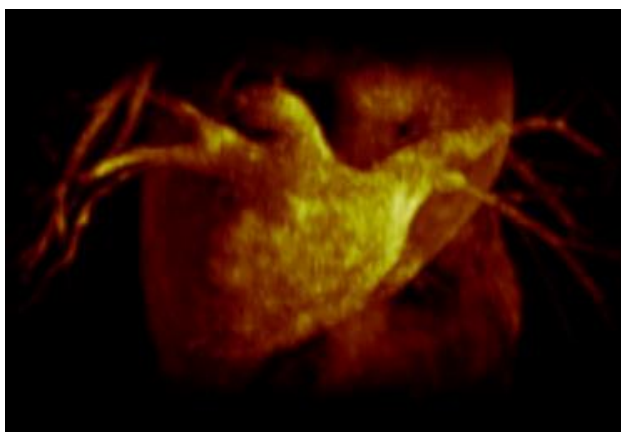
Figure 13. Examples of stress perfusion MRI pictures. Left: stress perfusion (stress induced ischemia in the inferior wall of the heart); Right: *LGE*.

### 3.2.4. Cardiac MRI before and after atrial ablation in therapy for Atrial Fibrillation

In cases of AF cardiac MRI is very helpful for planning atrial ablation therapy (pulmonary vein isolation (PVI)), as well as following up on the treatment success. At our hospital, we use it routinely prior to a planned ablation to measure the left atrium and general cardiac function, check for the anatomy of the pulmonary veins (PV) and assess possible left atrial fibrosis. In certain cases, we also use it early after the ablation (24 to 72 hours) to look for edema and possible stenoses of the pulmonary veins. Moreover, we scan our patients three months after the ablation as part of our routine treatment to examine the induced scars in the atrium, possible stenoses of the pulmonary veins and again measure the left atrium and cardiac function to evaluate the final ablation success. We always start with our standard sequences mentioned above, continue with giving a contrast agent and performing an angiography of the pulmonary veins by a *free breathing scan*. Finally, we do *3D-LGE* imaging (see 3.2.2) of the left atrium (LA) to evaluate the scarring in the LA. When performing MRI 24-72 hours after ablation, we additionally run a *T2* scan prior to giving contrast to best assess the edema after the procedure.

Localizer HASTE (Scan planning)	CINE LAX (function)	T2 (edema)	Contrast agent ↓ PV- angiography (angiography/ stenoses)	CINE SAX (function/ volumetry)	3D-LA- LGE (scarring)
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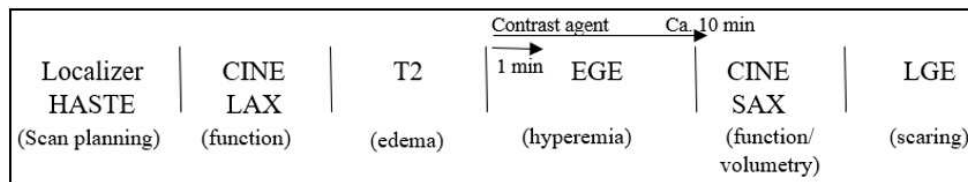
**Figure 14. PVI MRI protocol**



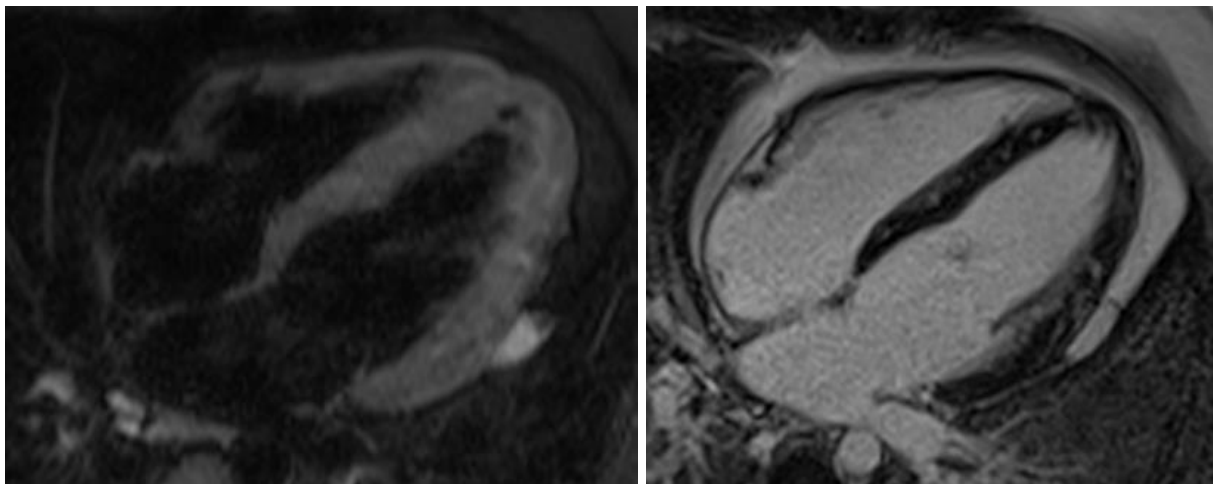
**Figure 15. Examples of PVI MRI pictures. Left: angiography; Right: LGE (showing LA fibrosis).**

### 3.2.5. Myocarditis Assessment

To assess for myocarditis, we basically use the same protocol as for acute viability testing with the addition of an early gadolinium enhancement (*EGE*) scan. In this case, we are scanning already one minute after contrast injection, when the contrast agent is just beginning to accumulate in the possibly inflamed myocardium. This process (hyperemia) is considered to be pathologically altered in inflammatory processes such as myocarditis. Together with *T2* and *LGE* imaging we gain valuable information to make a profound statement concerning the probability of myocarditis.



**Figure 16. Myocarditis MRI protocol**



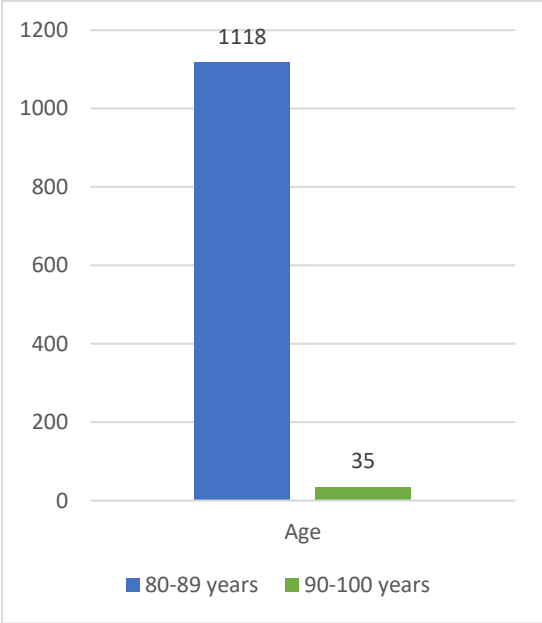
**Figure 17. Examples of myocarditis MRI pictures. Left: T2 weighted; Right: LGE (typical edema and intramural LGE pattern in myocarditis).**

### 3.3. Statistical Analysis

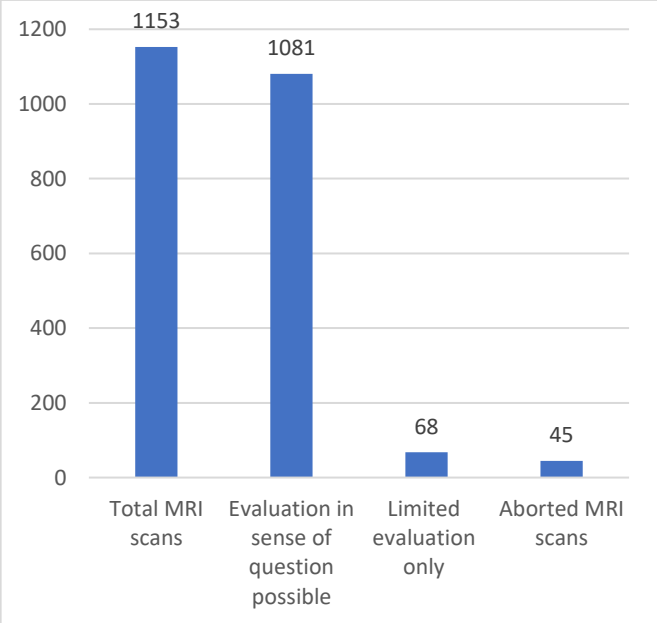
Statistical analysis was performed using IBM-SPSS version 23. Normal continuous variables are presented as mean  $\pm$  standard deviations. Categorical variables are presented as number and percentage of total.

## **4. RESULTS**

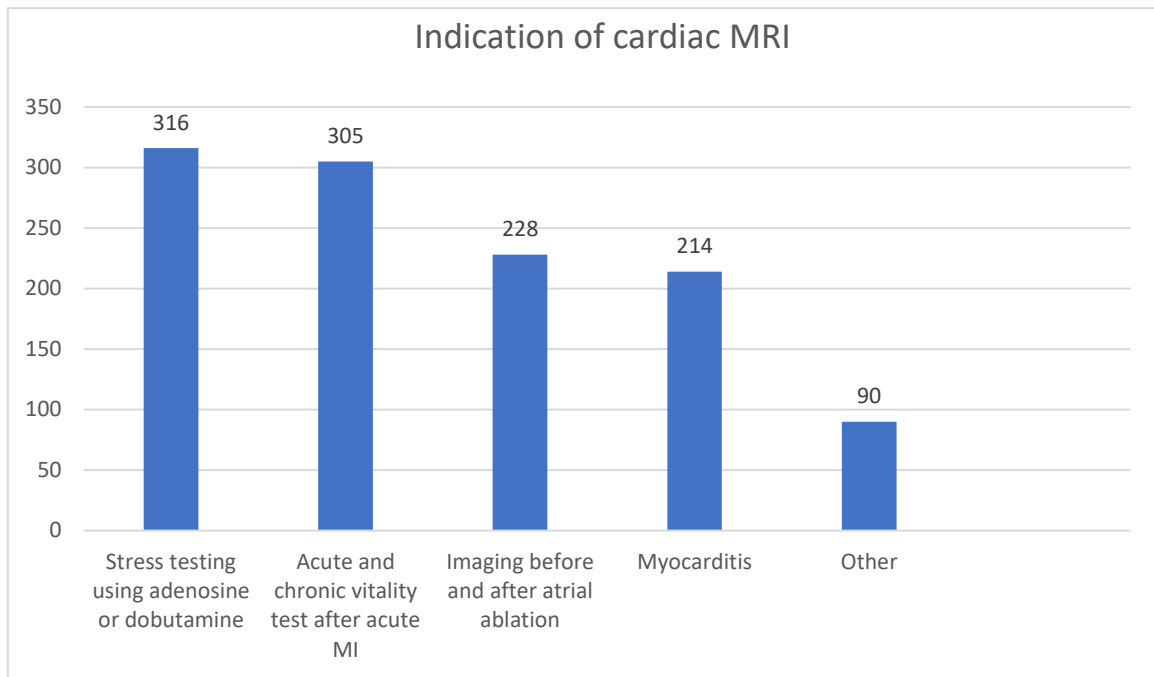
A total of 1153 patients (597 males (49.2%); 586 females (50.8%)), were included in the final analysis. Most patients were between 80 and 89 years old (1118; 97%), the lesser part  $\geq 90$  years (35; 3%, Figure 18). The main indications for cardiac MRI were stress testing using adenosine or dobutamine (27.4%; n=316), vitality tests acute or chronic after myocardial infarction (26.4%; n=305), imaging before and after ablation for atrial fibrillation (19.8%, n=228) and myocarditis (18.6%; n=214). The remaining MRI (7.8%) related to less common indications such as tumors, thrombus, or systemic diseases (Figure 20). A total of 45 (3.9%) of the MRI examinations were aborted early by the patients. An evaluation in the sense of the question was possible in 1081 (93.8%) of the patients. A limited ability to assess was found in 69 (6%) of the patients (Figure 19).



**Figure 18. Distribution of age groups**



**Figure 19. The total number of cardiac MRI, as well as those, that were assessable, limited assessable and aborted**



**Figure 20. Different indication for cardiac MRI in our study**

#### 4.1. Early termination of the MRI

Forty-five patients aborted the MRI. Among those were 27 (60%) females and 18 (40%) males. Mean age in the group of interrupted MRI scans was  $84.39 \pm 3.45$  years. Table 1 gives a summary of the reasons why the MRI was terminated early by the patients. Most common was according to the patients wish in 62.2% (n=28). In 15.6% the reason was not specified (n=7). In 6.7% patients complained of angina pectoris (AP) (n=3). Dyspnea, a non-compliant patient, and claustrophobia led to the abortion of the scans in 4.4% (n=2). Single reasons among the patients to terminate an MRI scan early were multiple artifacts detected already during the time the scans were taken, technical problems, comorbidities, errors in picture reconstruction and a detected contraindication for MRI (each 2.2%, n=1).



**Table 1. Reasons for early termination**

<b>Reason</b>	<b>Number of patients</b>	<b>Number in percent</b>
Patient's wish	28	62.2
Not specified	7	15.6
Angina Pectoris	3	6.7
Dyspnea	2	4.4
Non-Compliance	2	4.4
Claustrophobia	2	4.4
Technical problem	1	2.2
Comorbidities	1	2.2
Error in picture reconstruction	1	2.2
Contraindication for MRI	1	2.2
Multiple artifacts	1	2.2

#### 4.2. Cardio MRI examinations with limited assessability

A total of 68 patients had MRI with limited assessability. 28 (41.2%) of them were females and 40 (58.8%) were male. Mean age of these patients was  $83.04 \pm 2.82$ . Reasons are depicted in Table 2. Most common, was a bad imaging resulted due to non-compliant patients (52.9%; n=36). 22.1% of evaluations were complicated by arrhythmias (n=15), 16.2% by implants (n=11). Artifacts (e.g., movement or other kinds of artifacts) and dyspnea interfered with the interpretation in 5.9% (n=4), whereas pleural or pericardial edemas or general bad image quality only disturbed the clear evaluation in 4.4% (n=3). In 1.5% the area of interest was not clearly visible one the MRI or a decompensated heart insufficiency disturbed the clear picture. In 26.5% reasons were not clearly specified (n=18).

**Table 2. Reasons for limited assessability**

<b>Reason</b>	<b>Number of patients</b>	<b>Number in percent</b>
Non-compliance	36	52.9
No statement	18	26.5
Arrhythmia	15	22.1
Implants	11	16.2
Artifacts	4	5.9
Dyspnea	4	5.9
Edema (pleural, pericardial))	3	4.4
Bad image quality	3	4.4
Area of interest not visible	1	1.5
Decompensated heart insufficiency	1	1.5

## **5. DISCUSSION**

Due to demographic change patients in hospitals generally get older. This demographic trend especially in the western countries leads into advanced research focusing on diseases, diagnostic challenges, and treatment in the elderly population. Cardiovascular diseases are common in older patients. Forman *et al.* describe in their study of cardiovascular biomarkers and imaging, the need for adjusted normal ranges of biomarkers and problems with imaging in older patients due to more contraindications and movement artifacts and especially lacking data. These authors stated that cardiac MRI in elderly patients is difficult due to prolonged scanning times that compromise image quality due to motion artifact, precluded use of cardiac MRI due to implants, as well as limited usage of gadolinium contrast agent in end stage kidney disease. They also state that very limited data are available on test performance among patients with multiple comorbidities and that are over 75 years old (22). Our study focused on the feasibility of cMRI in old and very old people. In contrast to Forman *et al.* our main findings showed that cMRI is feasible in 96.1% of the patients over the age of 80. Furthermore, we found a 93.8% diagnostic reading ability in the sense of the diagnostic question. Only in 6% the ability to assess was limited. Another study conducted by Esteban-Fernandez *et al.* assessed the usefulness of stress MRI in patients over 70 years. They concluded that moderate to severe perfusion defects seen in stress MRI highly predicted cardiovascular events in people older than 70 years, without relevant adverse effects (34). Our current study is consistent with these earlier findings as we were able to show that cardiac MRI is feasible and promises a diagnostic benefit in elderly patients.

The indication for MRI during the hospitalization were in most cases stress testing with adenosine and dobutamine, acute and chronic viability testing after an acute MI, scans before and after atrial ablation and myocarditis. In less often cases the MRI checked for thrombi, tumors or systemic diseases. Bruder *et al.* describe among other the most common indications for a cardiac MRI in Europe according to the European cardiovascular magnetic resonance (EuroCMR) registry. The findings correlate with our results that the most common indication in Europe is risk stratification in suspected CAD or ischemia. In contrast to our study where viability assessment was the second most common indication, in Europe the next common indication for cardiac MRI are screening for myocarditis and cardiomyopathies (35). This can be explained as Bruder *et al.* included all patients in the registry whereas our study included only patients older than 80 years and myocarditis is more common in younger patients (36).

We also investigated the most common reasons why patients aborted the MRI. The most common reason was according to the patients wish, due to dyspnea or AP complaints and non-

compliance of the patient. Also less common reasons like claustrophobia, technical problems, comorbidities, errors in picture reconstruction or contraindications for MRI led to early abortion. In 4.4% no reason was classified. To our knowledge there has not yet been a similar study published in this area of focus. Further studies focusing on differences in age groups or gender, as well as a comparison of abortions of cardiac MRI in older versus in younger patients are needed to investigate this matter.

Another part of our study reviewed reasons for a limited assessability of the MRI. This was mostly due to non-compliance of the patients, arrhythmias, implants, artifacts, pleural / pulmonary effusion, movement artifacts, cardiac decompensation, area of interest not completely visible or bad image quality. In a few cases there was no reason named or not clearly specified (diverse). Most of the reasons we found in our study are described in the study of Forman *et al.* as limitations of cardiac MRI in elderly patients (22). Nonetheless, we found a limited ability to assess in only 6% of patients, which can lead to the conclusion that in contrast to what Forman *et al.* describe these factors are not a limitation for the majority of old and very old patients. Further research is needed in this area to investigate whether age or gender groups as well as possible effects of certain diseases have an impact on the ability to assess a cardiac MRI. Furthermore, further technical developments should focus on optimizing cardiac MRI in elderly people, since this vulnerable group of patients often wears devices, has more concomitant diseases such as pleural effusions and does not tolerate long examination times.

When interpreting and applying our conclusion, limitations must be considered. First is that this is a retrospective study which has no control group of younger patients which would have given a better insight of the feasibility of a cardiac MRI in elderly patients in comparison to these younger ones and some aspects may have gotten lost as they have not been gathered in first place. Another limiting factor is the fact that we haven't evaluated the quality of the MRI images ourselves and only read the reports of the MRI afterwards. However, this study took place in a certified cardiac center with very well trained and experienced cardiologists. Finally, this is a single center study. Nonetheless, the Department of Cardiology in Coburg treats several thousands of patients each year in every age group and thus, our study shows a good average of the population in this age group with regard to diseases due to the large catchment area.

## **6. CONCLUSIONS**

Our results indicate that cardiac MRI is a well usable diagnostic tool in old and very old patients because very few patients discontinue the examination early and only a few examinations are evaluable in a limited way. Most cardiac MRI examinations in this age group are stress testing, viability assessments, MRI before and after atrial ablation and myocarditis scans. Therefore, cardiac MRI should be considered for diagnostics in old and very old cardiovascular patients for an individual therapy decision in this vulnerable population.

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## **8. SUMMARY**

**Objectives:** Determination if cardiac MRI is a safe diagnostic tool regarding cardiac disease in everyday clinical practice in old and very old people. Additionally, this study aims to evaluate the validity of the diagnostic data obtained in the cardiac MRI.

**Materials and methods:** For this study, all patients over 80 years of age who received a cardiac MRI (3T Verio und 1,5T Espree, Siemens, Erlangen, Germany) between February 2014 and November 2021 as part of their inpatient treatment were analyzed retrospectively. The focus of our analysis was on the indication for the MRI, whether the MRI was terminated prematurely by the patient and whether the MRI could be evaluated regarding the medical question.

**Results:** A total of 1153 patients (567 male,  $82 \pm 2.9$  years) were included in the final analysis. The age range was between 80 and 100 years. Most patients were between 80 and 89 years old (1118; 97%), fewer patients  $\geq 90$  years (35; 3). The main indications for cardiac MRI were stress testing using adenosine or dobutamine (27.4%;  $n=316$ ), vitality tests acute or chronic after myocardial infarction (26.4%;  $n=305$ ), imaging before and after ablation for atrial fibrillation (19.8%,  $n=228$ ) and myocarditis (18.6%;  $n=214$ ). The remaining MRI (7.8%) related to less common indications such as tumors, thrombus or systemic diseases. A total of 45 (3.9%) of the MRI examinations were terminated prematurely by the patients. 27 (60%) were females and 18 (40%) males. Mean age in the group of interrupted MRI scans was  $84.39 \pm 3.445$ . Most common reasons were according to the patients wish in 62.2% ( $n=28$ ), 15.6% not specified ( $n=7$ ), 6.7% angina pectoris (AP) ( $n=3$ ), 4.4% dyspnea, non-compliance of patient, claustrophobia ( $n=2$ ), 2.2% multiple artifacts detected already during the time the scans were taken, technical problems, comorbidities, errors in picture reconstruction and a detected contraindication for MRI ( $n=1$ ). An evaluation in the sense of the question was possible in 1081 (93.8%) of the patients. A limited ability to assess was found in 69 (6%) of the patients. 28 (41.2%) of them were females and 40 (58.8%) were male. Mean age of these patients was  $83.044 \pm 2.8202$ . Most common reasons were in 52.9% non-compliance of patient ( $n=36$ ), 26.5% not clearly specified ( $n=18$ ), 22.1% arrhythmias ( $n=15$ ), 16.2% implants ( $n=11$ ), 5.9% artifacts (eg., movement or other kinds of artifacts) and dyspnea ( $n=4$ ), 4.4% pleural or pericardial edemas and general bad image quality, 1.5% the area of interest was not clearly visible on the MRI and decompensated heart insufficiency.

**Conclusion:** Our results indicate that cardiac MRI is a suitable diagnostic tool in old and very old patients because very few patients discontinue the examination early and only a few examinations are evaluable in a limited way. Most cardiac MRI examinations are stress testing,

viability assessments, before and after atrial ablation and myocarditis scans. Cardiac MRI should be considered for diagnostics in elderly cardiovascular patients as part of an individual therapy decision in this vulnerable population.

## **9. CROATIAN SUMMARY**

**Naslov:** Magnetska rezonanca srca – klinički podaci o izvedivosti i valjanosti u starijih i vrlo starih bolesnika

**Ciljevi:** Utvrđivanje je li MRI srca siguran dijagnostički alat za srčane bolesti u svakodnevnoj kliničkoj praksi u starijih i vrlo starih ljudi. Osim toga, ova studija ima za cilj procijeniti valjanost dijagnostičkih podataka dobivenih navedenom metodom.

**Materijali i metode:** Za ovu studiju retrospektivno su analizirani svi pacijenti stariji od 80 godina kojima je napravljen MRI srca (3T Verio und 1,5T Espree, Siemens, Erlangen, Njemačka) između veljače 2014. i studenog 2021. kao dio bolničkog liječenja. Fokus naše analize bio je na indikaciji za MRI, je li pacijent prerano prekinuo MRI i može li se MRI procijeniti s obzirom na medicinsko pitanje.

**Rezultati:** Ukupno 1153 bolesnika (567 muškaraca,  $82 \pm 2,9$  godina) uključeno je u konačnu analizu. Raspon godina bio je između 80 i 100 godina. Većina bolesnika bila je u dobi od 80 do 89 godina (1118; 97%), manjina bolesnika  $\geq 90$  godina (35; 3). Glavne indikacije za MRI srca bile su testiranje opterećenja adenzinom ili dobutaminom (27,4%;  $n=316$ ), akutni ili kronični testovi vitalnosti nakon infarkta miokarda (26,4%;  $n=305$ ), snimanje prije i poslije ablacije zbog fibrilacije atrijske (19,8% ,  $n=228$ ) i miokarditis (18,6%;  $n=214$ ). Preostali MRI (7,8%) odnosio se na manje uobičajene indikacije poput tumora, tromba ili sistemskih bolesti. Pacijenti su prerano prekinuli ukupno 45 (3,9%) MRI pregleda. 27 (60%) su bile žene i 18 (40%) muškarci. Prosječna dob u skupini prekinutih MRI pretraga bila je  $84,39 \pm 3,445$ . Najčešći razlozi bili su po želji bolesnika u 62,2% ( $n=28$ ), 15,6% nespecificirano ( $n=7$ ), 6,7% angina pectoris (AP) ( $n=3$ ), 4,4% dispneja, nepristajanje bolesnika , klaustrofobija ( $n=2$ ), 2,2% višestruki artefakti otkriveni već tijekom vremena snimanja, tehnički problemi, komorbiditeti, pogreške u rekonstrukciji slike i otkrivena kontraindikacija za MRI ( $n=1$ ). Procjena u smislu pitanja bila je moguća u 1081 (93,8%) pacijenata. Ograničena sposobnost procjene pronađena je u 69 (6%) pacijenata. Od toga je 28 (41,2%) žena i 40 (58,8%) muškaraca. Prosječna dob ovih pacijenata bila je  $83,044 \pm 2,8202$ . Najčešći razlozi bili su u 52,9% nesuradljivost pacijenata ( $n=36$ ), 26,5% nisu jasno navedeni ( $n=18$ ), 22,1% aritmije ( $n=15$ ), 16,2% implantati ( $n=11$ ), 5,9% artefakti (npr. pokreti ili druge vrste artefakata) i dispneja ( $n=4$ ), 4,4% pleuralni ili perikardijalni edemi i općenito loša kvaliteta slike, 1,5% područje interesa nije bilo jasno vidljivo na MRI i dekompenzirana srčana insuficijencija.

**Zaključci:** Naši rezultati pokazuju da je magnetska rezonanca srca prikladno dijagnostičko sredstvo u starijih i vrlo starih pacijenata jer vrlo mali broj pacijenata rano prekine pregled i samo je nekoliko pregleda moguće evaluirati na ograničen način. Većina MRI pregleda srca su testiranje opterećenja, procjena vitalnosti, prije i poslije ablacije atrijske i skeniranje miokarditisa.



MRI srca se kao dijagnostička metoda u starijih kardiovaskularnih bolesnika treba razmotriti kao dio individualne odluke o terapiji u ovoj ranjivoj populaciji.

## **10. CURRICULUM VITAE**

**Personal Data:**

Name: Laura Rebecca Hartnik

Date of birth: 12<sup>th</sup> of April 1997

Place of birth: Germany

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Since October 2016: Medical Studies in English at the Medical School Regiomed, a collaboration of the University of Split School of Medicine, Croatia and Regiomed Kliniken, Germany

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