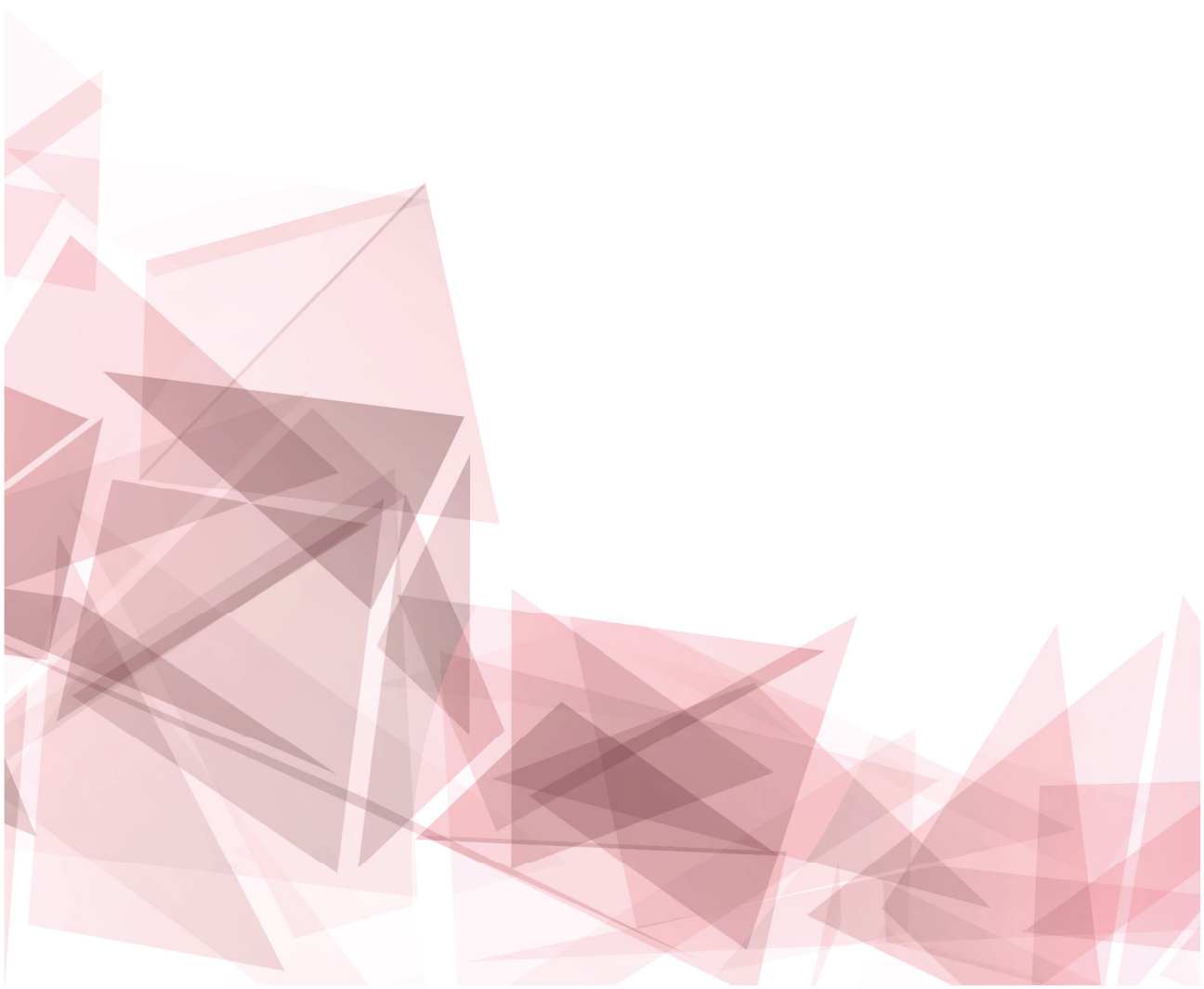
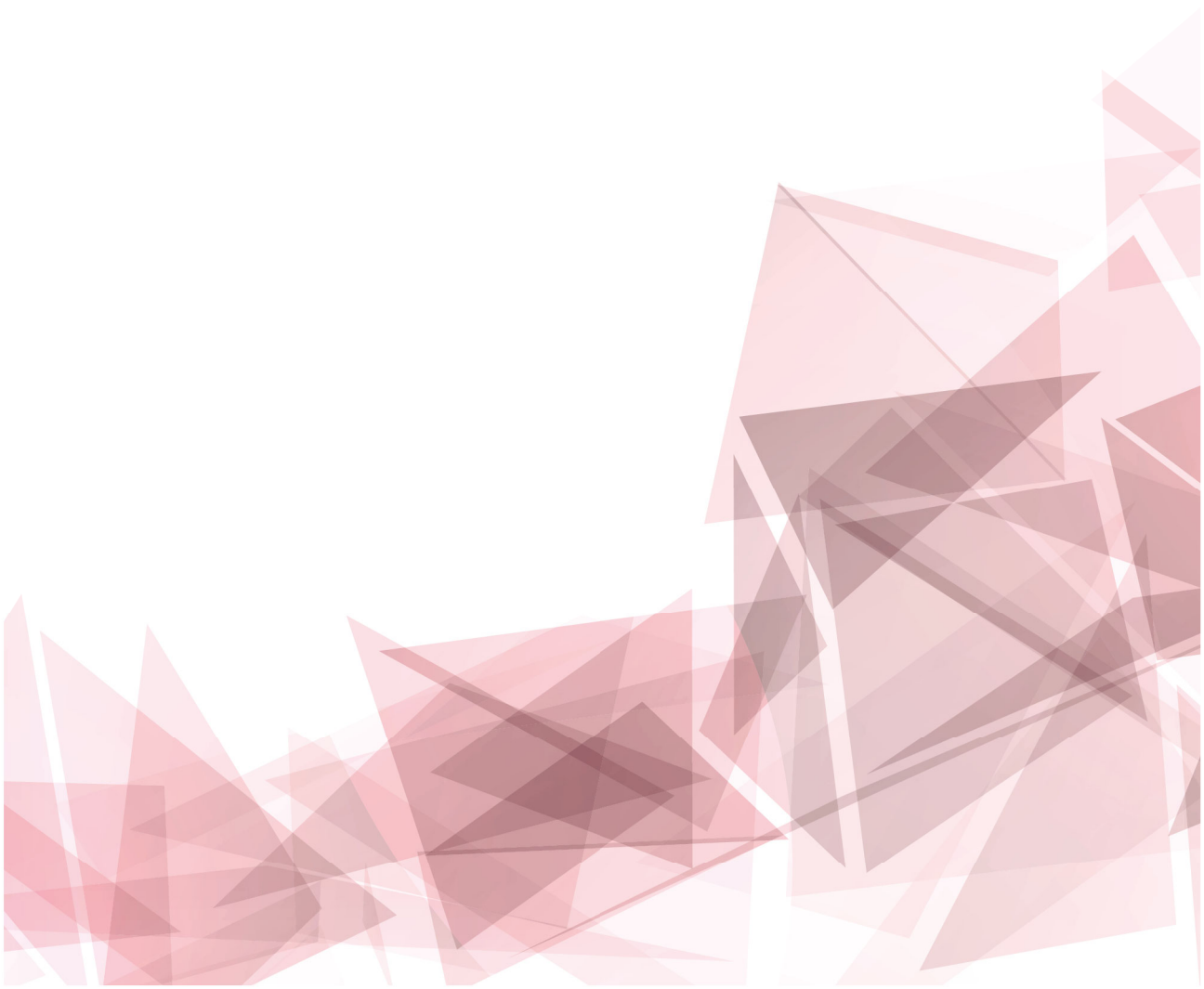
Cardiac imaging characteristics of patients with COPD: prognostic implications

Goedemans, L.



Summary, conclusions and future perspectives

Samenvatting, conclusies en toekomstperspectieven



Summary

The general introduction (**Chapter 1**) of this thesis provides an overview of the interaction between chronic obstructive pulmonary disease (COPD) and acute myocardial infarction (AMI), with a special focus on the role of cardiac imaging in risk stratification. Several complex pathological mechanisms, including shared risk factors and COPD specific characteristics such as hypoxia, explain the relationship between COPD and AMI. Also, the presence of acute exacerbation of COPD lead to an increased systemic inflammatory response, resulting in a higher risk of both type 1 and type 2 AMI. However, the role of elevated troponin T in acute exacerbations has still not been completely explored. When present, AMI in patients with COPD results in increased mortality, heart failure hospitalizations and arrhythmias. Conventional 2-dimensional echocardiography is the imaging technique of first choice for evaluating infarct size, left (LV) and right ventricular (RV) size and function. Besides, the role of advanced echocardiographic imaging techniques are introduced. Of these, speckle-tracking echocardiography allows to analyze left- and right ventricular longitudinal strain, as well as atrial strain, in order to provide further risk stratification in patients with COPD experiencing AMI. The current thesis aims at investigating the influence of COPD on cardiac function as assessed with echocardiography, in patients with ischemic heart disease (IHD) or atrial fibrillation. Furthermore, the prognostic implications of COPD in patients with cardiac disease and the role of imaging in risk stratification was evaluated.

Part I – Impact of COPD on left- and right ventricular function after acute myocardial infarction

In the first part of this thesis, the influence of COPD on LV and RV function after AMI is addressed. Both conventional and advanced echocardiographic techniques are used to evaluate differences between AMI patents with- and without COPD. Furthermore, the prognostic implications of LV global longitudinal strain (GLS) are discussed.

In patients experiencing ST-segment elevation myocardial infarction (STEMI), infarct size can be analyzed through measuring biomarkers (i.e. Troponine and Creatinine Kinase [CK]) or by echocardiographic evaluation of LV function. Conventional measures such as LV ejection fraction (LVEF) and wall motion score index (WMSI) might not be sensitive enough to characterize the extent of myocardial damage after STEMI, whereas advanced speckle tracking echocardiography derived LV GLS has emerged as a valuable index of LV function and infarct size. **Chapter 2** compares the differences in infarct size after STEMI between patients with and without COPD in a large cohort of patients treated with primary percutaneous intervention (PCI). Although biomarkers and conventional echocardiographic parameters indicated similar infarct size, a significantly more impaired

LV GLS was demonstrated in COPD patients. This indicates COPD patients might have worse LV function already in the early phase post-STEMI.

LV GLS measures the active contraction of the myocardium and directly reflects myocardial function. Recent literature has demonstrated that LV GLS is strongly associated with prognosis in patients with various cardiac diseases. In **Chapter 3**, the prognostic implications of LV GLS was evaluated in a study population of STEMI patients with concomitant COPD. The prognostic value of impaired LV GLS (defined as LV GLS >-14.4% [less negative]) was compared with conventional measures of LV- and right ventricular (RV) systolic function (i.e. LVEF, WMSI and tricuspid annular plane systolic excursion [TAPSE]). All-cause mortality was significantly worse in patients with more impaired LV GLS (>-14.4%). After correcting for clinically relevant factors (i.e. age, diabetes, β-blocker use) LV GLS >-14.4% was independently associated with all-cause mortality while LVEF, WMSI and TAPSE were not. Similar results were found for the combined endpoint consisting of all-cause mortality and heart failure admission. In addition, LV GLS >-14.4% had incremental prognostic value in a model containing clinical and conventional echocardiographic parameters for LV and RV function.

COPD is characterized by remodeling of the pulmonary vasculature, increased pulmonary vascular resistance and hypoxia. Subsequently, COPD is often accompanied by secondary pulmonary hypertension leading to pressure overload of the RV. Recently, RV involvement after STEMI has emerged as subject of debate in research and has important prognostic implications. In **Chapter 4**, the occurrence of RV systolic dysfunction was assessed in STEMI patients with and without COPD. RV dysfunction was assessed with conventional echocardiographic parameters (TAPSE <17 mm, RV fractional area change [FAC] <35%, tricuspid annular systolic excursion velocity [S'] <6 cm/s) and advanced speckle tracking echocardiography derived RV free wall longitudinal strain (RV FWSL) >-20%. RV dysfunction manifested more frequently in patients with COPD, mainly when analyzed with RV FWSL. Furthermore, RV FWSL >-20% was independently associated with 5-year all-cause mortality in the total population and showed to be of incremental prognostic value in a model containing clinical parameters and LVEF. On the contrary, conventional parameters for RV dysfunction were not associated with 5-year all-cause mortality. Therefore, RV FWSL might be a more sensitive prognostic marker after STEMI, particularly in patients with COPD.

Part II – Influence of COPD on the development of atrial arrhythmias

In the second part of this thesis, the influence of COPD on the development of atrial arrhythmias and the characterization of atrial function in COPD patients is highlighted.

COPD is an important risk factor for development of atrial fibrillation (AF) in the general population. Similarly, up to 20% of patients experiencing AMI develop AF either during the acute phase or at follow-up. Prior to the development of AF, patients might

already show increased supraventricular activity resulting in atrial tachycardia (AT) or excessive supraventricular ectopy activity (ESVEA). Previous studies have demonstrated an increased incidence of AF in patients with ESVEA and AT. An increased risk of stroke was even observed in patients with ESVEA without known AF. **Chapter 5** evaluates a population of STEMI patients following a yearly protocol of regular 24 hour Holter ECG's and outpatient visits, allowing close monitoring for the development of arrhythmias. Patients with and without COPD were compared with regards to the occurrence of AT, ESVEA and AF during one year follow-up. In particular the incidence of AT was significantly higher in COPD patients (70%) when compared to non-COPD patients (46%). Also, ESVEA was observed more often in COPD patients (21% vs. 11%, $p<0.05$). On the contrary, the incidence of AF was similar in both groups. Multivariate analysis indicated COPD to be independently associated with the development of any atrial arrhythmia during 1 year follow-up after STEMI. At long term, no differences in AF development were observed although the data might show an underestimation of the true incidence due to loss of follow-up. These results indicate that close clinical monitoring after STEMI is warranted, most particularly in patients with COPD. This might lead to timely discovery of atrial arrhythmias warranting therapeutic intervention (i.e. anticoagulation).

Although COPD is a known risk factor for development of AF, only few studies have been performed to identify the underlying substrate. Atrial remodeling is a key feature in AF and is associated with treatment success and adverse events. Previous literature has been dedicated to structural remodeling of the left atrium. However, it has been indicated that right atrial foci for AF are more common in patients with COPD. Right sided pressure overload due to secondary pulmonary hypertension in COPD is thought to be one of the underlying mechanisms. **Chapter 6** describes differences in left- and right atrial size and function in AF patients with- and without COPD. For this, both conventional echocardiographic measurements as well as advanced echocardiography derived atrial strain, representing atrial stiffness and fibrosis, were retrieved. When compared to healthy individuals, AF patients have significantly impaired left- and right atrial reservoir strain. Interestingly, left atrial volumes and function were similar in patients with and without COPD while right atrial strain was significantly more impaired in COPD patients. Additionally, a tendency towards worse RA function with increasing COPD severity was observed in small groups of patients. These data support the potentially considerable role of the right atrium in AF development in patients with COPD.

Conclusions and future perspectives

The impact of COPD on cardiac function is of clinical importance and significance, particularly in patients with AMI. COPD not merely affects prognosis by worse LV function but also RV function is significantly affected. Thorough evaluation of cardiac function with both conventional and advanced echocardiography is vital in order to provide adequate

risk stratification. COPD patients could have a higher benefit from patient tailored management after cardiac events.

COPD patients have a more impaired LV GLS after STEMI when compared to patients without COPD. Similarly, RV FWSL assessment could help to identify more patients with RV dysfunction. Both parameters have important prognostic implications with regard to heart failure and all-cause mortality. Future prospective studies using these advanced echocardiographic measurements could be helpful to identify COPD patients with subtle LV- and RV dysfunction prior to the first cardiac event. Furthermore, when following these patients prospectively, the impact of cardiac events on LV- and RV function could answer the question whether these patients are more vulnerable for ischemia. Besides, larger study populations would be crucial to evaluate differences in cardiac function in patients with different stages of COPD. This is of clinical relevance since COPD patients could be referred earlier for cardiac evaluation and frequent monitoring during follow-up after cardiac events could provide better secondary prevention.

Besides IHD, COPD patients are more prone to develop atrial arrhythmias both after ischemic events and in the overall population. Structural atrial remodeling, particularly of the right atrium, is suggested to be an important pathophysiologic substrate. Future research should be dedicated to determine the role of the right atrium in the development of AF in COPD patients, whilst current therapeutic interventions are mainly focused on the left atrium. Echocardiography may provide an additional tool in characterization of atrial structure and function. Furthermore, prospective studies addressing regular outpatient monitoring of arrhythmias could help to identify patients at highest risk, subsequently leading to timely and targeted therapeutic intervention.