ABSTRACT

Objective: We aimed to find the prevalence and the reasons for receiving non-guideline-concordant treatment in patients with multivessel coronary artery disease (mv-CAD), at a single centre.

Methods: All consecutive patients who underwent coronary angiography, due to stable angina pectoris or non-ST-elevation acute coronary syndrome (NSTEMI-ACS), and were diagnosed with mv-CAD at our hospital between August 2017 and February 2018 were included in this study. Stand-alone medical treatment, percutaneous coronary intervention (PCI), coronary artery bypass grafting (CABG), or hybrid revascularization is recommended treatment methods by The European
1. INTRODUCTION

Decision-making for patients with multivessel coronary artery disease (mv-CAD) is a complex process for physicians and patients. Multiple factors, such as previous experience, scientific knowledge and media facilities, may have significant impacts on the decision process. Physicians and patients may have different perceptions and anticipations about treatment. Current myocardial revascularisation guidelines provide comprehensive recommendations for appropriate revascularisation methods in patients with mv-CAD. However, implementing these recommendations in real life is a challenging task [1,2].

Previous studies reported that inappropriate coronary revascularisation prevalence, especially for non-acute conditions, is high and resulted in poor outcomes [3–5]. However, these trials included not only patients with mv-CAD but also patients with single-vessel CAD. The decision-making process for patients with the single-vessel disease is usually straight forward. On the other hand, the decision-making process is more demanding for patients with mv-CAD. A ‘Heart Team’, including interventional and non-interventional cardiologists and cardiac surgeons, is recommended for the treatment decision process [6]. The patient and the patient’s family preference should also be taken into consideration.

The PCI-to-CABG ratio has increased significantly more towards PCI procedures [7–9]. Even within the same health care system, a large difference in PCI-to-CABG ratios has been reported across different regions [10,11]. Contemporary data on the appropriateness of coronary revascularisation for patients with mv-CAD is limited. Since the decision-making process is influenced by many factors, in this study, we aimed to find the reasons for and the prevalence of receiving non-guideline-concordant treatment in patients with mv-CAD, at a single-centre.

2. METHODS

All consecutive patients who underwent coronary angiography, due to stable angina pectoris or non-ST-elevation acute coronary syndrome (NSTE-ACS), and were diagnosed with mv-CAD at our hospital between August 2017 and February 2018, were included in this cross-sectional, observational study. For this study, mv-CAD was defined as follows: Isolated or non-isolated unprotected left main CAD (stenosis ≥50%), 70% or greater stenosis in a left anterior descending artery (LAD) and 70% or greater stenosis in at least one other major epicardial vessel, with invasive or non-invasive proof of ischaemia.

Coronary artery stenosis severity was assessed with Quantitative Coronary Analysis. The syntax I and Syntax II Scores were calculated for all patients. Stand-alone medical treatment, percutaneous coronary intervention (PCI), coronary artery bypass grafting (CABG) or hybrid revascularisation are recommended treatment methods for appropriate patients and conditions by The European Society of Cardiology (ESC) and The European Association for Cardio-
Thoracic Surgery Guidelines (EACTS) on Myocardial Revascularisation.

The concordance of the treatment method, with the guideline, was determined by two independent cardiologists who did not participate in the treatment decision process. Guideline-concordant treatment and non-concordant treatment were defined as follows: a) Two-vessel disease with proximal LAD stenosis (concordant: PCI or CABG, non-concordant: stand-alone medical treatment), b) Left main disease with a SYNTAX score ≤32 (concordant: PCI or CABG, non-concordant: PCI or stand-alone medical treatment), c) Left main disease with a SYNTAX score ≥33 (concordant: CABG, non-concordant: PCI or stand-alone medical treatment), d) Three-vessel disease with a SYNTAX score ≤22 (concordant: CABG or PCI, non-concordant: stand-alone medical treatment), e) Three-vessel disease with a SYNTAX score >22 (concordant: CABG, non-concordant: PCI or stand-alone medical treatment), f) Three vessel disease, diabetes mellitus and SYNTAX scores ≤22 (concordant: CABG or PCI, non-concordant: PCI or stand-alone medical treatment), g) Three vessel disease, diabetes mellitus and SYNTAX score >22 (concordant: CABG, non-concordant: PCI or stand-alone medical treatment) and h) Patients with chronic heart failure and systolic LV dysfunction (ejection fraction ≤35% and presence of viable myocardium, concordant: CABG, non-concordant: PCI or stand-alone medical treatment). According to the guidelines, a Heart Team should consider the following aspects for deciding between CABG and PCI among patients with stable mv-CAD and/or left main CAD: Presence of severe co-morbidity (not adequately reflected by scores), advanced age/frailty/reduced life expectancy, restricted mobility and conditions that affect the rehabilitation process, anatomy likely resulting in incomplete revascularisation with CABG due to poor quality or missing conduits, severe chest deformation or scoliosis, sequelae of chest radiation or porcelain aorta that favours PCI, contraindication to dual antiplatelet therapy, recurrent diffuse in-stent restenosis, anatomy likely resulting in incomplete revascularisation with PCI, severely calcified coronary artery lesions limiting lesion expansion, ascending aortic pathology with indication for surgery and concomitant cardiac surgery that favours CABG.

Patients who refused to participate had undergone a previous CABG, NSTE-ACS patients with ongoing angina, haemodynamic deterioration or refractory arrhythmias were excluded. Stabilised NSTE-ACS patients were assessed as stable angina pectoris patients due to the recommendation of the guidelines. Patients who refused recommended treatment and, therefore discharged, were queried by telephone to determine whether they received guideline-concordant treatment or another method within 30 days following coronary angiography.

Since we could not access and assess the decision-making procedure that occurred between the patient and the physician, initially, we classified the reasons of receiving non-guideline treatment as ‘patient preference/cardiologist decision’, thereafter we performed a further interview with physicians and patients to learn the reasons for the treatment decision.

Economic status was defined as follows: low (income per four family members is less than minimum wage), intermediate (income per four family members is between 1–3 minimum wages) and high (income per four family members is more than 3 minimum wages). The most current ESC and EACTS myocardial revascularisation guidelines were released after we completed patient recruitment [2]. Therefore, we reviewed all patients according to the recommendations of the new guidelines. The study complied with the principles of the Declaration of Helsinki, and the local Ethics Committee approved the study protocol.

2.1 Statistical Analysis

Continuous variables were presented as mean ± standard deviation or median (25%–75% percentiles), and categorical variables were expressed as number and percentage (%). The Kolmogorov-Smirnov test was used to identify normally distributed variables. The continuous variables were compared across the groups using the Student’s t-test or the Mann-Whitney U test. The categorical variables were compared using the chi-square or Fisher’s exact tests. All the data were analysed with SPSS v16.0 for Windows (SPSS Inc., Chicago, IL, USA). A p-value <0.05 was considered statistically significant.

3. RESULTS

A total of 140 patients (96 male, 68.6% and 111 NSTE-ACS, 79.3%) were included in
this study, of which 65 (46.4%) received non-guideline-concordant, whereas 75 (53.6%) received guideline-concordant treatment. Sociodemographic and clinical characteristics did not differ statistically between patients who received guideline-concordant treatment and non-guideline-concordant treatment. Left ventricular ejection fraction (LVEF) were higher \((p=0.017)\), and SYNTAX I score \((p<0.001)\) and SYNTAX II score for PCI \((p<0.001)\) were significantly lower in the guideline-concordant treatment group (Table 1). The reasons for receiving non-guideline-concordant treatment were that the patient preferred and/or the cardiologist selected PCI over CABG \((42, 64.6\%)\), the patient refused treatment with any revascularisation method \((14, 21.5\%)\), the surgeons refused to perform the operation despite the initial decision of the ‘Heart Team’ \((5, 7.7\%)\), the surgery team was unavailable \((1, 1.5%)\) and the patient developed ischaemia/myocardial infarction during the waiting period \((3, 4.6\%)\) (Table 2). There was no inappropriate CABG decision. Of the 42 patients who underwent non-guideline-concordant PCI, 23 \((54.7\%)\) received ad-hoc PCI and 11 \((26\%)\) received PCI at another hospital. Of the 14 patients who did not undergo revascularisation treatment, 3 \((21.4\%)\) had undergone angiography a few years ago and had also refused revascularisation treatment at that time.

A query to further understand the basis for the treatment decisions revealed that patients received non-guideline-concordant treatment (available for 56 patients) for the following reasons: fear of an open surgery \((38, 68\%)\), keeping surgery as a final treatment \((12, 21\%)\), refusing the severity of the disease \((6, 11\%)\) (Table 3). The reasons declared by physicians were as follows (available for 47 patients): assessed the severity of the disease as lower than it actually was \((18, 38\%)\), assessed the risk for surgery as higher than it actually was \((16, 34\%)\), concerns about performance-based income \((7, 15\%)\) and lack of confidence in the surgery team \((6, 13\%)\) (Table 4).

### 4. DISCUSSION

In this study, we found that almost half of the patients with mv-CAD did not receive guideline-concordant coronary revascularisation. This prevalence is higher than previously reported. However, previous studies classified procedures as appropriate, inappropriate or uncertain and they included both single vessel CAD and mv-CAD \([3–5, 12]\). Therefore, the inappropriateness rates of these studies might be higher than reported. We did not find any significant differences regarding sociodemographic and clinical characteristics between the two patient groups to explain this high prevalence. In our study, we assumed that the high prevalence of receiving non-guideline-concordant coronary revascularisation may have been associated primarily with interventional cardiologists.

Current ESC revascularisation guidelines recommend a multidisciplinary decision-making process by a ‘Heart Team’ and recommend predefining an institutional protocol for patients with mv-CAD. Physician-related factors may significantly influence treatment decisions. Cardiac surgeons and cardiologists may create a bias towards a specific treatment \([13]\). Chandrasekharan et al. reported that 68% of patients were not aware of an alternative revascularisation method \([14]\). All members of the team should be actively involved in the discussion, and decision-making should occur in a non-autocratic and non-hierarchical setting. Although leadership is crucial for a team, decision-making by autocratic physicians may create bias \([15]\).

**Table 1. Baseline characteristics of the patients**

<table>
<thead>
<tr>
<th></th>
<th>Group 1 Non-guideline-concordant</th>
<th>Group 2 Guideline-concordant</th>
<th>(P)</th>
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</thead>
<tbody>
<tr>
<td><strong>Non-guideline-concordant ((n=65))</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>65 ± 11</td>
<td>62 ± 8.5</td>
<td>0.113</td>
</tr>
<tr>
<td>Male gender n (%)</td>
<td>41 (63.1)</td>
<td>54 (72.0)</td>
<td>0.260</td>
</tr>
<tr>
<td><strong>Economic level</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>25 (38.5)</td>
<td>34 (45.3)</td>
<td>0.644</td>
</tr>
<tr>
<td>Intermediate</td>
<td>27 (41.5)</td>
<td>27 (36.0)</td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>13 (20.0)</td>
<td>14 (18.6)</td>
<td></td>
</tr>
<tr>
<td><strong>Living Area</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urban</td>
<td>43 (66.2)</td>
<td>44 (58.7)</td>
<td>0.628</td>
</tr>
<tr>
<td>Reason</td>
<td>n (%)</td>
<td></td>
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<tr>
<td>----------------------------------------------------------------------</td>
<td>---------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient’s preference and/or cardiologist’s decision of PCI rather than CABG</td>
<td>42 (64.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient’s refusal of any revascularization method</td>
<td>14 (21.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Operation refusal by surgeons*</td>
<td>5 (7.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Developing ischemia/myocardial infarction during waiting period</td>
<td>3 (4.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unavailability of surgery team</td>
<td>1 (1.5)</td>
<td></td>
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</tbody>
</table>

*Refusal by surgeons due to relatively high mortality risk or incooperation about surgery with patient and/or patients’ family, or technical difficulties

Table 3. The reasons of non-guideline-concordant treatment declared by patients (available for 56 patients)

<table>
<thead>
<tr>
<th>Reason</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fear of an open surgery</td>
<td>38 (68)</td>
</tr>
<tr>
<td>Keeping surgery as a final treatment</td>
<td>12 (21)</td>
</tr>
<tr>
<td>Refusing the severity of the disease</td>
<td>6 (11)</td>
</tr>
</tbody>
</table>

Table 4. The reasons of non-guideline-concordant treatment declared by physicians (available for 47 patients)

<table>
<thead>
<tr>
<th>Reason</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assessing the severity of the disease as lower than it is</td>
<td>18 (38)</td>
</tr>
<tr>
<td>Assessing the risk for surgery as higher than it is</td>
<td>16 (34)</td>
</tr>
<tr>
<td>Concerns about performance based income</td>
<td>7 (15)</td>
</tr>
<tr>
<td>Lack of confidence to the surgery team</td>
<td>6 (13)</td>
</tr>
</tbody>
</table>

Ad-hoc PCI is the recommended strategy for patients with acute coronary syndromes. However, ad-hoc PCI for complex multivessel or unprotected left main CAD should be performed after a rapid surgical consultation or when CABG is indisputably an inappropriate preference, and the patient has been fully informed about benefits and risks of the procedure [16]. In our study, half of the non-guideline-concordant group received ad-hoc PCI. Although ad-hoc PCI is convenient for patients and interventional cardiologists and more cost-effective, it obviously increases the inappropriate revascularisation rates [17]. On the other hand, elective procedures may allow physicians to inform patients about their disease severity and accessibility to alternative treatment...
methods. Patients with coronary artery disease receive more recommendations for PCI and fewer recommendations for CABG surgery [14,18]. Despite the high prevalence of inappropriate ad-hoc PCI, there was no inappropriate CABG decision in our study. Ad-hoc PCI created a bias towards PCI in our study.

Patient preference should be considered, and patients should take active participation in the decision-making process. Moreover, involvement of patients’ families and friends in the heart team can increase patient satisfaction [19]. Conversely, patients often make decisions about medical treatments without a complete understanding of their conditions and options. Patients should be provided evidence-based information about treatment options and encouraged to use the information to make decisions without ignoring their values, preferences and lifestyle [20–22]. Videos of real patient perspectives regarding a particular treatment may help patients in the decision process [23]. When the patient's preference is discordant with the recommended treatment, the physician should use clinical judgment, combined with insightful communication with the patient, to obtain the best route for the patient [16]. A study by Kipp et al. hypothesised that patients prefer multivessel PCI (mv-PCI) instead of CABG even when informed of the high mv-PCI I risk [24]. Finally, they found that patients preferred mv-PCI over CABG, even when the risk of death was double the risk with CABG or the risk of repeat procedures was more than three times that for CABG (p<0.0001).

Nearly one in ten patients refused to undergo any revascularisation method in our study. Of these patients, three had a previous angiography, with a CABG surgery decision. However, these patients might be in denial regarding their cardiac illness or fear the revascularization procedures. Denial or fear leading to delayed treatment may have hazardous results. It has been reported that about one in three acute medical inpatients did not have the capacity to make a key, significant decisions about their treatment [25].

Surgery refusal by the surgery team, despite the initial CABG decision, was another important finding of our study. In a study by Waldo et al., surgical ineligibility was common in patients undergoing elective PCI [26]. Surgical ineligibility was associated with an increased risk of inhospital (OR: 6.26, 95% CI: 2.16–18.15, p <0.001) and long-term mortality (HR: 2.98, 95% CI: 1.88–4.72, p <0.001) after PCI. In another study, McNulty et al. found that most patients undergoing non-emergent, unprotected left main PCI were ineligible for CABG as an alternative [27]. Long term outcomes were worse for these patients. Therefore, treatment decisions for patients with complex CAD, who are ineligible for CABG, should be made by a ‘Heart Team’.

The timing of the CABG is another significant issue for patients with complex CAD. In our study, three patients underwent emergent PCI due to developing acute ischaemia or infarction within a week of the initial CABG decision. Although revascularization for patients with complex CAD is recommended to be performed within 2 weeks following diagnostic coronary angiography, these patients should be closely monitored for ischaemia/infarction and arrhythmias that might develop during the waiting period [28].

The additional interview for revealing reasons of non-guideline-concordant treatment showed that the physicians may have concerns about performance-based income. In a recent study by Robert et al., performance-based income did not improve the health of patients and may result in worsened outcomes for sicker and poorer patients, and moreover, may cause some doctors to stop using lifesaving treatments [29]. Adherence to guidelines is crucial and seems to be associated with an improved outcome [30]. In our study, we found that physicians’ adherence to guidelines was low and patients preferred the less invasive procedure.

We believe that measures should be taken by occupational associations and health ministries to improve the physicians’ adherence to guidelines. On the other hand, effective and rational use of media facilities by health managers may play a role in informing patients about appropriate treatments.

5. STUDY LIMITATIONS

We conducted a single centre study. Our results may only show local practice and experience. Therefore, the results cannot be generalised to the entire country. We included patients with stable coronary artery disease and patients with ‘stable’ NSTE-ACS. Although these conditions have many similarities, they are not precisely the same. Our patient number was relatively small and we unintentionally might have made selection bias during the grouping of patients.
6. CONCLUSION

To the best of our knowledge, this is the first report from Turkey about the prevalence and short-term mortality of non-guideline-concordant treatment in patients with mv-CAD. Prevalence of non-guideline-concordant treatment was high in our study. Implementing a ‘Heart Team’ and performing multivessel procedures with two separate catheterisations may increase guideline-concordant treatment.

ETHICAL APPROVAL

The study complied with the principles of the Declaration of Helsinki, and the local Ethics Committee approved the study protocol.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

13. Head SJ, Bogers AJ, Serruys PW, Takkenberg JJ, Kappetein AP. A crucial


