Original Research Article

Reasons of Non-guideline-concordant Treatment in Patients with Multivessel Coronary Artery Disease. REGRET-ONE TRIAL

abstract

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

Methods: All consecutive patients who underwent coronary angiography due to stable angina pectoris or non-ST-elevation acute coronary syndrome (NSTE-ACS) and diagnosed to have mv-CAD at our hospital between August 2017 and February 2018, prospectively included in this study. Standalone medical treatment, percutaneous coronary intervention (PCI), coronary artery bypass grafting (CABG) or hybrid revascularization are recommended treatment methods by The European Society of Cardiology (ESC) and The European Association for Cardio-Thoracic Surgery Guidelines (EACTS) on Myocardial Revascularization. Stabilized NSTE-ACS patients were assessed as stable angina pectoris patient

Results: Overall 140 patients (96 male, 68.6% and 111 NSTE-ACS, 79.3%) prospectively included in this study. Of these, 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. The reasons of receiving non-guideline-concordant treatment were patient's preference and/or cardiologist's decision of PCI over CABG (42, 64.6%), patient's refusal of any revascularization method (14, 21.5 %), operation refusal by surgery team due to advanced patient age or low left ventricular ejection fraction (5, 7.7%) unavailability of surgery team (1,

1.5%), developing ischemia/myocardial infarction during waiting period (3, 4.6 %). There was no inappropriate CABG decision.

Conclusions: Prevalence of non-guideline-concordant treatment was high and associated primarily with interventional cardiologists and patients' preferences in our study.

Introduction

Decision-making for patients with multivessel coronary artery disease (mv-CAD) is a complex process for physicians and patients. Multiple factors like previous experience, scientific knowledge, media facilities may have significant impacts on the decision process. Physicians and patients may have different perceptions and anticipations about treatment. Current myocardial revascularization guidelines provide comprehensive recommendations for appropriate revascularization 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 revascularization prevalence, especially for non-acute conditions, is high and with poor outcomes (3-5). However, these trials included not only patients with mv-CAD, but also patients with single vessel CAD. Decision making process for patients with single-vessel disease is usually straightforward. On the other hand, decision making process is more demanding for patients with mv-CAD. A 'Heart Team' including interventional and non-interventional cardiologists, cardiac surgeons is recommended for treatment decision process (6). Patient and patient's family preference also should take into consideration.

PCI-to-CABG ratio has increased significantly towards more 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 appropriateness of coronary revascularization for patients with mv-CAD is limited. Since decision-making process is influencable from many factors, in this study

we aimed to find the reasons, prevalence of receiving non-guideline-concordant treatment in patients with mv-CAD at a single-center.

Methods

All patients who underwent coronary angiography due to stable angina pectoris or non-ST-elevation acute coronary syndrome (NSTE-ACS) and diagnosed to have mv-CAD at our hospital between August 2017 and February 2018, consecutively included in this study. The study was cross-sectional and observational. For the purpose of this study mv-CAD was defined as follows: Isolated or non-isolated unprotected left main CAD (stenosis ≥50%), 70% or greater stenosis in 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 ischemia.

Coronary artery stenosis severity was assessed with Quantitative Coronary Analysis. 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 revascularization 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 Revascularization.

The concordance of 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: a)Two-vessel disease with proximal LAD stenosis (concordant:PCI or CAGB, non-concordant:standalonemedical treatment), b) Left main disease with a SYNTAX score ≤32 (concordant:PCI or CABG, non-concordant: standalone medical), c) Left main disease with a SYNTAX score ≥33 (concordant:CABG, non-concordant: PCI or standalone medical treatment), d)Three-vessel disease with a SYNTAX score ≤ 22 (PCI or CABG), e) Three-vessel disease with a SYNTAX score ≤22 (concordant:CABG or PCI, nonconcordant: standalone medical treatment),f)Three-vessel disease with a SYNTAX score >22 (concordant: CABG, nonconcordant: PCI

or standalone medical treatment g) Three vessel disease, diabetes mellitus and SYNTAX score≤22(concordant: CABG or PCI, non-concordant: standalone medical treatment) h)Three vessel disease, diabetes mellitus and SYNTAX score>22 (concordant: CABG, non-concordant: PCI or standalone medical treatment)i)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 guideline Heart Team considered following aspects for decision-making between CABG and PCI among patients with stable multivessel and/or left main coronary artery disease: 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 revascularization with CABG due to poor quality or missing conduits, severe chest deformation or scoliosis, sequelae of chest radiation porcelain aorta favour PCI, on the other hand contraindication to dual antiplatelet therapy, recurrent diffuse in-stent restenosis, anatomy likely resulting in incomplete revascularization with PCI, severely calcified coronary artery lesions limiting lesion expansion, ascending aortic pathology with indication for surgery, concomitant cardiac surgery favour CABG.

Patients who refused to participate, with previous CABG, NSTE-ACS patients with ongoing angina or deteriorated hemodynamics or refractory arrhythmias were excluded. Stabilized NSTE-ACS patients were assessed as stable angina pectoris patients due to relevant recommendation of the guideline. Patients who refused recommended treatment and 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 occurred between patient and 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 find the reasons.

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

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 analyzed with SPSS v16.0 for Windows (SPSS Inc., Chicago, IL). A p- value <0.05 was considered to be statistically significant.

Results

Overall 140 patients (96 male, 68.6% and 111 NSTE-ACS, 79.3%) prospectively included in this study. Of these, 65 (46.4%) received non-guideline-concordant (group 1) whereas 75 (53.6%) received guideline-concordant treatment (group 2). Sociodemographic and clinical characteristics did not differ statistically between patients who received guideline-concordant treatment and non-guideline-concordant treatment. LVEF were higher (p=0.017), SYNTAX I score (<0.001) and SYNTAX II score for PCI (<0.001) were significantly lower in the guideline-concordant treatment group (Table 1).The reasons of receiving non-guideline-concordant treatment were patient's preference and/or cardiologist's decision of PCI over CABG (42, 64.6%), patient's refusal of any revascularization method (14, 21.5 %), operation refusal by surgeons despite initial decision of Heart Team(5, 7.7%),

unavailability of surgery team (1, 1.5%), developing ischemia/myocardial infarction during waiting period (3, 4.6 %) (Table2). There was no inappropriate CABG decision. Of 42 patients who underwent non-guideline-concordant PCI 23 (54.7%) received ad-hoc PCI and 11 (26%) received PCI at another hospital. Of 14 patients who did not admit any revascularization method 3 (21.4%) had undergone angiography a few years ago and had refused revascularization treatment once more.

In a further query to reveal the details, the reasons of non-guideline-concordant treatment declared by patients (available for 56 patients) were as follows: fear of an open surgery (38, 68%), keeping surgery as a final treatment, refusing the severity of the disease (12, 21%), fear of recurrence of the disease (6, 11%) (Table 3). The reasons declared by physicians were as follows (available for 47 patients): assessing the severity of the disease as lower than it is (18, 38%), assessing the risk for surgery as higher than it is (16, 34%), concerns about performance based income (7, 15%), lack of confidence to surgery team (6, 13%) (Table 4).

Discussion

In this study, we found that almost half of the patients with mv-CAD did not receive guideline-concordant coronary revascularization. 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, inappropriateness rates of these studies might be higher than reported. We did not find any significant difference regarding sociodemographic and clinical characteristics between two patient groups to explain this high prevalence. We assume that the high prevalence of receiving non-guideline-concordant coronary revascularization in our study may be associated primarily with interventional cardiologists.

Current ESC revascularization guideline recommends a multidisciplinary decision-making process by a Heart Team and recommends 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). In a study Chandrasekharanet al

reported 68% of patients were not aware of an alternative revascularization method (14). All members of team should actively involve in 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).

Ad-hoc PCI is the recommended strategy for the 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 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 revascularization rates (17).On the other hand, elective procedures may allow physicians informing patients about their disease severity and accessibility of alternative treatment methods. Patients with coronary artery disease receive more recommendations for PCI and fewer recommendations for CABG surgery (14, 18). Despite 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 taken into account and patients should take active participation in decision process. Moreover, involvement of patients' families and friends in the heart team can increase patient satisfaction (19). On the other hand, 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 the particular treatment may help patients in decision process (23). When patient preference discordant with recommended treatment, the physician should use clinical judgment combined with insightful communication with the patient to obtain best route for the patient (16). In a study Kipp et al hypothesized patients prefer multivessel PCI (mv-PCI)

instead of CABG even when quoted high mv-PCI 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 any revascularization method in our study. Of these patients three had a previous angiography with a CABG decision. However, these patients might be in a denial of cardiac illness or in a fear of revascularization procedures. Denial or fear leading delays in receiving treatment may have hazardous results. It is reported that about one in three acute medical inpatients did not have capacity to make key significant decisions about their treatment (25).

Operation refusal by surgery team despite initial CABG decision was another important finding of our study. In a study Waldo et al reported that surgical ineligibility is common in patients undergoing elective PCI. (26). Surgical ineligibility was associated with an increased risk of in-hospital (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 nonemergent 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.

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 ischemia or infarction within a week of 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 monitorized for new developing ischemia/infarction and arrhythmia (28).

The further interview for the revealing of reasons of non-guideline-concordant treatment showed that the physicians may have concerns about performance based income. In a recent study Roberst

et al reported that performance based income did not improve the health of patients and may harm sicker and poorer patients and moreover may cause stop some doctors 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 ministry to improve the physicians' adherence to guidelines. On the other hand, effective and rational use of media facilities by health managers may play role to inform patients about appropriate treatments.

Study limitations

We conducted a single center study. Our results may only show local practice and experience. The results cannot be generalized to all 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 low and unintentionally we might have made selection bias during grouping patients.

Conclusions:

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 catheterizations may increase guideline-concordant treatment.

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Table 1: Baseline characteristics of the patients

	Group 1 Non-guideline-concordant (n=65)	Group 2 Guideline-concordant (n=75)	P
Age	65 ± 11	62 ± 8.5	0.113
Male gender n (%)	41(63.1)	54 (72.0)	0.260

Economic level			
Low	25 (38.5)	34 (45.3)	0.644
Intermediate	27 (41.5)	27 (36.0)	
High	13 (20.0)	14 (18.6)	
Living Area			
Urban	43 (66.2)	44 (58.7)	0.628
Rural	22 (33.8)	31 (41.3)	
Education level			
Illiterate	39 (60.0)	49 (65.3)	0.509
Primary school	21 (32.3)	18 (24.0)	
High School / University	5 (7.7)	8 (10.7)	
NSTE-ACS	54 (83.1)	57 (87.7)	0.303
Diabetes mellitus	30 (46.2)	28 (37.3)	0.291
Peripheral Arterial disease	6 (9.2)	4 (5.3)	0.372
Chronic kidney disease	3 (4.6)	2 (2.7)	0.535
Current Smoker	19 (29.2)	26 (34.7)	0.492
Family history of CAD	11 (16.9)	10 (13.3)	0.533
Systolic BP	139 ± 21	138 ± 22	0.920
Diastolic BP	84 ± 13	83 ± 12	0.613
LVEF	48 ± 8	52 ± 7	0.017
Diseased vessel	2.9 ± 0.5	2.9 ± 0.6	0.879
SYNTAX1	22.1 ± 6.3	17.7 ± 6.4	<0.001
SYNTAX 2 (for PCI)	37.4 ± 9.3	30.9 ± 7.9	<0.001
SYNTAX 2 (for CAGB)	25.3 ± 9	25 .8 ± 7.9	0.303

Table 2: Reasons of receiving non-guideline concordant treatment

Reason	n,%

Patient's preference and/or cardiologist's decision of PCI rather than CABG	42 (64.6)
Patient's refusal of any revascularization method	14 (21.5)
Operation refusal by surgeons*	5 (7.7)
Developing ischemia/myocardial infarction during waiting period	3 (4.6)
Unavailability of surgery team	1 (1.5)

*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)

Reason	n (%)
Fear of an open surgery	38 (68)
Keeping surgery as a final treatment	12 (21)
Fear of recurrence of the disease	6 (11)

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

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