Decision making in Ischemic cardiomyopathy: variability in physicians' approaches and patients' adherence

Toma de decisiones en la miocardiopatía isquémica: variabilidad en los enfoques de los médicos y la adherencia de los pacientes

Mostafa Bahremand[1], Taha Ahmadinejad[2], Yaser Jenab[2], Seyed Kianoush Hoseini[3], Masoumeh Lotfi-Tokaldany[4], Arash Jalali[5]*
[1]Cardiology Department, Kermanshah University of Medical Sciences, Kermanshah, Iran, https://orcid.org/0000-0002-1351-7039
[2]Cardiology Department, Tehran Heart Center, Tehran University of Medical Sciences, Tehran, Iran, https://orcid.org/0000-0002-8737-3146, https://orcid.org/0000-0002-8291-8637
[3]Cardiology Department, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran, https://orcid.org/0000-0001-9111-8941
[4]Research Department, Tehran Heart Center, Tehran University of Medical Sciences, Tehran, Iran, https://orcid.org/0000-0001-8222-8794
[5]Clinical Research Department, Tehran University of Medical Sciences, Tehran, Iran, https://orcid.org/0000-0002-7263-4745
**corresponding author: Yaser Jenab, MD, Cardiology Department, Tehran Heart Center, Tehran University of Medical Sciences, Tehran, Iran, Email: yasjenab@gmail.com*

Abstract

Ischemic cardiomyopathy (ICM) is a common cardiovascular disease with conflicting evidence regarding its management and a high risk profile for revascularization procedures that seems to have resulted in variable approach of physicians toward its management, and likewise, significant patient non-adherence to physician recommendation. We included patients with 3-vessel disease and left ventricular ejection fraction (LVEF) <45%(ICM group; n=825), and patients with LM disease and LVEF ≥45% (LM group; n=162), detected by coronary angiography at Tehran Heart Center. Variation of recommendations among cardiologists was evaluated. The rate of coronary artery bypass graft (CABG) non-adherence was also determined, as well as its predictors and outcome in ICM group. Decision making was more variable in ICM group, compared to LM group. CABG non-adherence was significantly more common in ICM group (32.4%), compared to LM group (10.0%) (P<0.001). Advanced age, being female, absence of angina, creatinine >2$^{mg/dl}$, severe left ventricular dysfunction, absence of LM disease and moderate or severe mitral regurgitation were predictors of CABG non-adherence. ICM patients with CABG non-adherence had significantly more all-cause mortality (Hazard Ratio [HR]: 1.97, 95% confidence interval [CI]: 1.28-3.04), and more all-cause mortality, revascularization or hospitalization due to cardiac disease (HR: 1.94, 95% CI: 1.41-2.67), than those who received CABG. While ICM is a common disorder encountered frequently in daily practice of cardiologists, there is a significant variability in decision making, as well as a significant non-adherenceto lifesaving recommendations for these patients.

Keywords: clinical decision making, patient adherence, cardiomyopathies, myocardial ischemia, left ventricular dysfunction, coronary artery bypass.

Resumen

La cardiomiopatía isquémica (ICM) es una enfermedad cardiovascular común con pruebas contradictorias con respecto a su manejo y un perfil de alto riesgo para los procedimientos de revascularización que parece haber resultado en un enfoque variable de los médicos hacia su manejo, e igualmente, una importante falta de adherencia del paciente al médico recomendación. Se incluyeron pacientes con enfermedad de 3 vasos y fracción de eyección del ventrículo izquierdo (FEVI) <45% (grupo ICM; n = 825), y pacientes con enfermedad LM y FEVI ≥45% (grupo LM; n = 162), detectados por enfermedad coronaria Angiografía en el Centro del Corazón de Teherán. Se evaluó la variación de las recomendaciones entre los cardiólogos. También se determinó la tasa de no adherencia del injerto de derivación de la arteria coronaria (CABG), así como sus factores predictivos y el resultado en el grupo de ICM. La toma de decisiones fue más variable en el grupo ICM, en comparación con el grupo LM. La falta de adherencia de CABG fue significativamente más común en el grupo ICM (32,4%), en comparación con el grupo LM (10,0%) (P <0,001). La edad avanzada, ser mujer, ausencia de angina, creatinina> 2 mg / dl, disfunción ventricular izquierda severa, ausencia de enfermedad LM y regurgitación mitral moderada o grave fueron factores predictores de no adherencia de CABG. Los pacientes con ICM con no adherencia de CABG tuvieron significativamente más mortalidad por todas las causas (relación de riesgo [HR]: 1.97, 95% intervalo de confianza [IC]: 1.28-3.04), y más mortalidad por todas las causas, revascularización u hospitalización debido a enfermedad cardíaca (HR: 1.94, IC 95%: 1.41-2.67), que aquellos que recibieron CABG. Si bien la ICM es un trastorno común que se encuentra con frecuencia en la práctica diaria de los cardiólogos, existe una variabilidad significativa en la toma de decisiones, así como

una importante no adherencia a las recomendaciones de salvamento para estos pacientes.

Palabras clave: toma de decisiones clínicas, adherencia del paciente, cardiomiopatías, isquemia miocárdica, disfunción ventricular izquierda, derivación coronaria.

Introduction

Coronary artery disease (CAD) has become a global epidemic of cardiovascular disease in 21st century. Ischemic cardiomyopathy (ICM), defined as myocardial dysfunction secondary to ischemic heart disease, is an ultimate consequence of CAD associated with a significant morbidity and mortality. Evaluating viability of myocardium first, recommending only medical treatment, or directly proceeding with Coronary Artery Bypass Graft (CABG) or Percutaneous Coronary Intervention (PCI) are different approaches used for the management of these patients. Unfortunately, conflicting results of several randomized and nonrandomized studies about the role of CABG[1,2] and viability study[3], and paucity of evidence about the role of PCI in the management of ICM[3,4] have resulted in a great uncertainty about the optimal approach to these patients. Furthermore, the unfavorable outcome of revascularization in these patients compared to patients with preserved left ventricular (LV) function, may result in reluctance of physicians to aggressively pursue these lifesaving procedures. These two factors can lead to inconsistent physicians' approach toward management of ICM and probably, under-recommendation of revascularization by physicians or its refusal by patients. We performed this study to evaluate two main objectives: first, how uniformly cardiologists make recommendation to patients with ICM, and second, how perfectly these recommendations are adhered to by patients. Since CABG is the only procedure with evidence supporting its survival benefit in ICM, we only evaluated adherence to CABG in patients with CABG recommendation to reduce complexity. To have a better concept, we compared consistency in recommendation and adherence to CABG recommendation in ICM patients, to patients with left main (LM) disease, who have stronger evidence supporting CABG for their management1without increased risk for cardiac surgery[5].We also sought to evaluate two secondary objectives: to scrutinize probable reasons for patient non-adherence we determined its predictors and to define its importance, we determined outcome of not adhering to CABG recommendation.

Materials and methods

Among all patients undergoing elective or emergency coronary angiography in Tehran Heart Center (THC), a tertiary referral hospital, from March 2007 through February 2008, we included patients with three vessel disease (3VD, i.e. at least one >50% visual stenos is of the luminal diameter of coronary arteries in all three main territories) and left ventricular ejection fraction (LVEF) <45% in LV angiography, with or without LM disease (ICM group). We also included another group with LM disease (>50% visual stenos is) and LVEF≥45% (LM group). LVEF mentioned in echocardiography report was considered when LV injection had not been performed. We excluded patients with previous history of CABG or PCI, as well as patients with congenital heart disease. Case selection was performed during June 2012.

As mentioned before, this study was performed to evaluate two main and two secondary objectives:

Defining variation in decision making. Angiographies were performed by 15 cardiologists, including 7 interventional cardiologists. First recommendation of the caring cardiologist, documented on angiography report, consisted of four options: ischemia/viability study, medical treatment, CABG or PCI. The proportion of each of these recommendations was determined for each cardiologist, as well as their range and standard deviation among all cardiologists.

Determining the rate of CABG non-adherence. Non-adherence was defined as not undergoing CABG within 1 year after angiography, despite physician recommendation. Patients undergoing CABG within 1 year, but after a cardiac event or PCI, were considered as non-adherence. THC medical records and databanks were scrutinized to ascertain whether CABG was or was not performed. When CABG status could not be ascertained by this way, it was determined by phone contact with patients or their families. Medical records and databank review as well as phone contacts, were made during September 2012 through March 2013. Patients whose CABG status could not be ascertained by either way, were excluded from analysis in this and the next two parts.

Patients died in the same admission within 5 days from angiography without revascularization, were assumed high risk or critically ill patients with no chance for revascularization and were also excluded from analysis.

The prevalence of CABG non-adherence in ICM patients was defined, and compared to LM patients.

Defining predictors of CABG non-adherence. Demographic and clinical variables of patients were extracted from THC databanks. These databanks contain data col-

lected for each patient at the time of angiography on a standard form, as a part of patient care process. Echocardiographic variables were also extracted from databanks, if it was performed at the time of angiography, as well as angiographic variables. These variables were evaluated as possible predictors (Table 1).

Data extraction was performed during July through August 2012.

Defining outcome of CABG non-adherence. Outcome of ICM patients with CABG recommendation who had undergone CABG within 1 year, was compared to those who had not. The primary outcome was all cause mortality within the follow-up period. The combined secondary outcome was all cause mortality, revascularization (CABG after 1 year from angiography or PCI) or hospital admission due to cardiac disease.

We collected data regarding mortality, revascularization, and hospital admission, using THC medical records and databanks. For patients with less than two years of follow up by this way, these data were collected by phone contact with patients or their families. Mortality data was completed and confirmed by data from the National Organization for Civil Registration, during April 2013.

Variables are presented as mean ± standard deviation (SD) for continuous variables or frequency and percentage for categorical variables. The proportions of four possible recommendations are presented as percentage, and their range and standard deviation were determined. Variation in decision making of different cardiologists, as well as rates of CABG non-adherence, among ICM and LM groups were compared using chi-square statistics. Patient characteristics were compared among patients who did or did not receive CABG, using T-test statistics for continuous variables and chi-square statistics for categorical variables. Independent predictors for CABG non-adherence in ICM patients were defined using backward logistic regression model. Variables with P value <0.2 were entered in the model. Variables with P value <0.1 were considered as independent predictors. The effects of independent predictors of CABG non-adherence in the final model are presented as odds ratio (OR) and 95% confidence intervals (CI).The area under the Receiver Operating Characteristic (ROC) curve was utilized to measure the model discrimination. The Hosmer-Leme show goodness-of-fit statistic was used to estimate the model calibration. Outcome comparison was performed using Cox's proportional hazards model with adjusting for confounding factors. The adjusted associations are expressed as hazard ratio (HR) and 95% CI. Variables simultaneously associated with both CABG adherence and mortality with P value<0.2 were considered as possible confounders. Plots for probability of primary and secondary outcome were estimated using Kaplan-Meier method after adjusting for confounding factors.

Table 1. Demographic, clinical, echocardiographic and angiographic variables evaluated as possible predictors of CABG non-adherence

Demographic variables	Past history of cerebrovascular disease	Serum creatinine	Angiographic variables
Age*	Past history of peripheral vascular disease	Echocardiographic variables	LV function†††
Sex	Past history of chronic obstructive lung disease	LV size**	Left main disease‡‡‡
Marital status†	Family history of CAD	RV size††	Severe stenos is of proximal LAD (>70%)
Education years‡	Diabetes mellitus	RV function‡‡	Number of main vessels with >70% stenos is§§§
Clinical variables	A trial fibrillation rhythm	MR§§	Number of target vessels with poor runoff****
Body mass index*	Drug history of Aspirin	Moderate or severe valvular disease other than MR	
Presence of angina		Pulmonary artery systolic pressure ***	
NYHA functional class§			
MI within 1 month			

* Were considered as continuous variables.
† Single, or married.
‡ 5 or less, 6 to 12, or 13 or higher.
§New York Heart Association functional classification of angina or dyspnea as I to IV.
** Not dilated, or dilated, defined as LV diastolic diameter ≥54^{mm} in women and ≥60^{mm} in men, in parasternal long axis view.
††Not dilated, or dilated, defined as mid RV diameter >34^{mm}.
‡‡Normal, or with dysfunction, defined as tricuspid annular plane systolic excursion <16^{mm} or RV systolic motion <10$^{cm/s}$in tissue Doppler.
§§ No or mild, moderate, or severe, assessed visually and defined in echocardiography report, or if not available, in angiography report.
*** Normal, or elevated, defined as estimated pressure >40^{mmHg}, mentioned in echocardiography report.
†††Normal or mildly impaired (LVEF ≥45%), moderately impaired (30%≤ LVEF <45%), or severely impaired (LVEF <30%).
‡‡‡ No or mild (<50% stenosis), moderate (50-70% stenosis), or severe (>70% stenosis).
§§§No, one, two, or three.
**** No, one, two,or three or more. Runoff of target vessels was determined in four territories: left anterior descending, diagonal, obtuse marginal and right coronary arteries. Target vessel diameter <1.5^{mm} or >70% stenosis after the usual site for graft anastomosis was defined as poor runoff.
MI = Myocardial Infarction; CAD = Coronary Artery Disease; LV = Left Ventricular; RV = Right Ventricular; MR = Mitral Regurgitation; LAD = Left Anterior Descending artery.

Results: Of all patients undergoing coronary angiography at THC during the mentioned period, 987 patients were included after applying inclusion and exclusion criteria. 825 patients in ICM group and 162 patients in LM group.

How variably physicians make recommendation to ICM and LM patients?

First recommendation of the caring cardiologist in the angiography report, was missing for nine ICM patients and one LM patient. The proportion of each off of our possible recommendations was determined for each cardiologist. They are demonstrated for ICM and LM patients in Table 2. Decision making for ICM patients was significantly more variable (P<0.001), compared to LM patients (P=0.658). For example, while four cardiologists have recommended CABG to more than 80% of their ICM patients, two cardiologists have recommended it in less than 60%. In contrast, all cardiologists have recommended CABG to more than 85% of their LM patients, whereas 10 cardiologists have recommended it to 100% of patients.

How commonly patients adhered to CABG recommendation?

In ICM patients, first recommendation was CABG for 582 out of 825patients (70.5%).CABG status within 1 year, could not be ascertained for 22 patients. Four patients had died without CABG, within 5 days from angiography in the same admission, and were excluded. Among remainders, 376 patients (67.6%) had undergone CABG within 1 year from coronary angiography, while 180 patients (32.4%) had not (Figure 1).

CABG was recommended for 156 out of 162 patients in LM group (96.3%). CABG status within 1 year, could not be verified for 6 patients. Overall, 135 patients (90.0%) had undergone CABG (all within 1 year), while 15 patients (10.0%) had never received the procedure (Figure 2).CABG non-adherence was significantly more common in ICM patients with respect to LM patients (P<0.001).

Table 2. Proportions of four possible recommendations, determined for each cardiologist, for patients with ICM and LM disease

	First Recommendation									
	ICM					LM disease				
Cardiologist Name	PCI%	CABG%	Medical%	Viability%	Total%(n)	PCI%	CABG%	Medical%	Viability%	Total%(n)
A	2.6%	71.8%	11.5%	14.1%	100%(78)	0.0%	100.0%	0.0%	0.0%	100%(13)
B	13.0%	69.6%	17.4%	0.0%	100%(23)	0.0%	85.7%	14.3%	0.0%	100%(7)
C	13.3%	70.0%	13.3%	3.3%	100%(30)	12.5%	87.5%	0.0%	0.0%	100%(8)
D	1.8%	64.9%	19.3%	14.0%	100%(57)	0.0%	100.0%	0.0%	0.0%	100%(11)
E	4.8%	80.6%	11.3%	3.2%	100%(62)	0.0%	100.0%	0.0%	0.0%	100%(17)
F	4.8%	64.3%	21.4%	9.5%	100%(42)	0.0%	100.0%	0.0%	0.0%	100%(2)
G	4.1%	59.5%	20.3%	16.2%	100%(74)	0.0%	100.0%	0.0%	0.0%	100%(11)
H	6.7%	75.6%	15.6%	2.2%	100%(45)	0.0%	100.0%	0.0%	0.0%	100%(6)
I	6.2%	71.6%	12.3%	9.9%	100%(81)	0.0%	90.9%	9.1%	0.0%	100%(11)
J	6.0%	84.5%	6.0%	3.6%	100%(84)	5.9%	94.1%	0.0%	0.0%	100%(17)
K	4.3%	82.6%	8.7%	4.3%	100%(23)	0.0%	100.0%	0.0%	0.0%	100%(9)
L	6.3%	71.4%	15.9%	6.3%	100%(63)	0.0%	96.7%	3.3%	0.0%	100%(30)
M	4.4%	86.7%	8.9%	0.0%	100%(45)	0.0%	100.0%	0.0%	0.0%	100%(8)
N	0.0%	71.4%	28.6%	0.0%	100%(28)	0.0%	100.0%	0.0%	0.0%	100%(4)
O	4.9%	55.6%	17.3%	22.2%	100%(81)	0.0%	100.0%	0.0%	0.0%	100%(7)
Total	5.1%	71.3%	14.6%	8.9%	100%(816)	1.2%	96.9%	1.9%	0.0%	100%(161)
Range	13.3%	31.1%	22.6%	22.2%		12.5%	14.3%	14.3%	0.0%	
SD	3.6%	8.9%	5.8%	6.8%		3.5%	5.0%	4.2%	0.0%	

Fifteen cardiologists are coded as A to O. ICM = ischemic cardiomyopathy; LM = left main; PCI = Percutaneous Coronary Intervention; CABG = Coronary Artery Bypass Graft; SD = Standard Deviation

Figure 1. Adherence to CABG recommendation in ICM patients

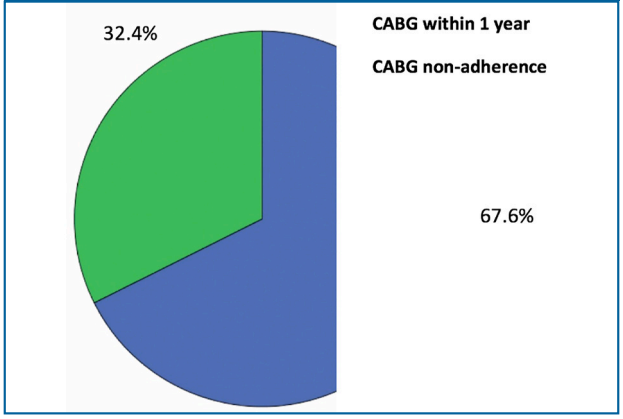


Figure 2. Adherence to CABG recommendation in LM patients

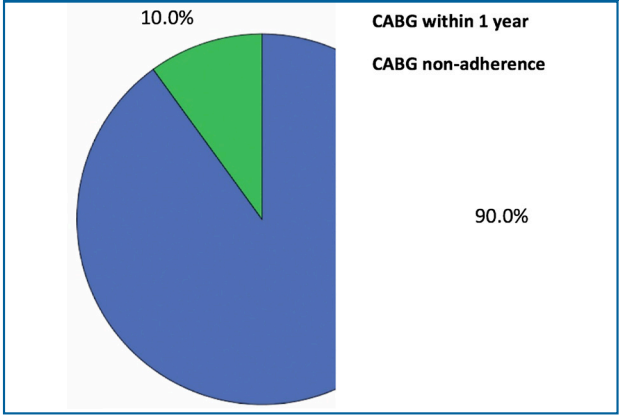


Table 3. Independent predictors of CABG non-adherence

		CABG within 1 year			
		Yes (n=376)	**No** (n=180)		
		n(%) or mean(±SD)	n(%) or mean(±SD)	P value	OR(95% CI)
Age		60.19±9.87	64.01±10.66	0.000	1.05 (1.02-1.07)
Marital Status	Married	334(69.4%)	147(30.6%)	0.032	0.47 (0.24-0.94)
	Not married	33(52.4%)	30(47.6%)		
Angina NYHA FC II-IV	Yes	166(73.8%)	59(26.2%)	0.055	0.61 (0.37-1.01)
	No	210(63.4%)	121(36.6%)		
Serum Creatinine	<2$^{mg/dl}$	365(69.5%)	160(30.5%)		
	≥2$^{mg/dl}$	11(36.7%)	19(63.3%)	0.012	3.21 (1.29-8.02)
LV Function	Moderately impaired	330(70.8%)	136(29.2%)		
	Severely impaired	46(51.1%)	44(48.9%)	0.032	1.92 (1.06-3.50)
Left Main Disease	No or mild	314(65.7%)	164(34.3%)		
	Moderate	41(74.5%)	14(25.5%)	0.044	0.41 (0.17-0.98)
	Severe	21(91.3%)	2(8.7%)	0.062	0.13 (0.02-1.10)
MR	No or mild	282(71.6%)	112(28.4%)		
	Moderate	80(61.5%)	50(38.5%)	0.002	2.26 (1.35-3.80)
	Severe	14(43.8%)	18(56.2%)	0.002	3.64 (1.58-8.40)

Area under the ROC curve: 0.789; Hosmer-Lemeshow goodness-of-fit: P=0.32.
CABG = Coronary Artery Bypass Graft; NYHA FC = New York Heart Association Functional Class; LV = Left Ventricular; MR = Mitral Regurgitation.

What are predictors of CABG non-adherence?

After stepwise logistic regression analysis, independent predictors of CABG non-adherence within 1 year were advanced age, serum creatinine more than 2$^{mg/dl}$, severe LV dysfunction and moderate or severe MR, while being married, presence of angina and moderate or severe left main disease had negative correlation with CABG non-adherence.

Does CABG non-adherence influence outcomes?

Mortality (dead or alive), revascularization (CABG, PCI or none) and admission data were collected using phone contact or THC medical records. Mortality data was confirmed and completed by data from the National Organization for Civil Registration. The mean ± SD follow up time, was 39.1±19.6 months for primary outcome and 31.1±18.8 months for secondary outcome. All-cause mortality was lower for ICM patients with CABG recommendation who received the procedure within 1 year, compared to those who did not (13.3% vs. 41.4%, P <0.001). After adjusting for confounding factors in Cox's proportional hazards model, CABG non-adherence patients still had significantly higher all-cause mortality than CABG patients (HR: 2.01, 95% CI: 1.31-3.09) (Figure 3). CABG non-adherence patients, also had significantly greater all-cause mortality, revascularization or admission due to cardiac disease, compared to CABG patients, after adjusting for confounding factors (HR: 1.91, 95% CI: 1.39-2.63) (Figure 4).

Figure 3.Probability of all-cause mortality in ICM patients with CABG recommendation who did and did not receive CABG

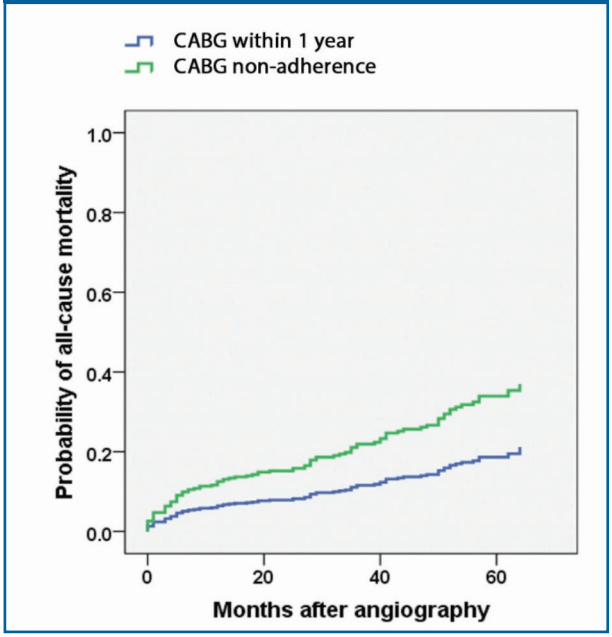
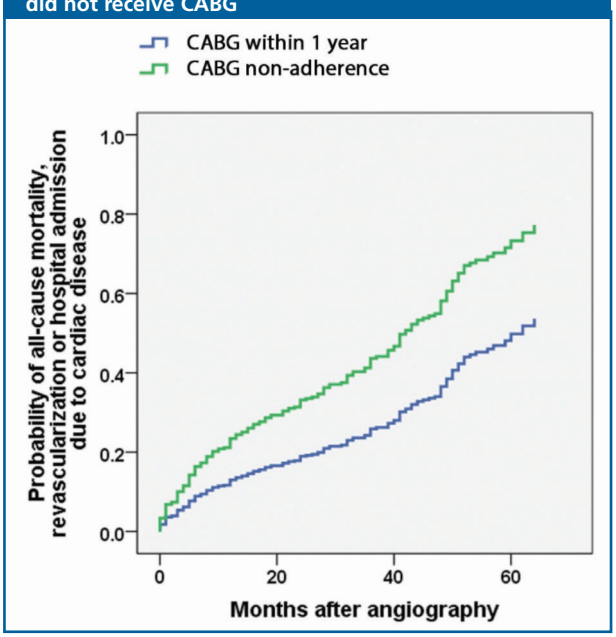


Figure 4.Probability of all-cause mortality, revascularization or admission due to cardiac disease in ICM patients with CABG recommendation who did and did not receive CABG



Discussion

In this study, we demonstrated that there is significant variation in decision making of individual physicians for ICM patients. We also found that a significant number of ICM patients with CABG recommendation, do not receive the procedure. This variation in decision making as well as CABG non-adherence, is significantly greater in ICM patients compared with LM patients. Furthermore, patients who did not receive CABG despite physician recommendation, had a significantly worse outcome than patients who did.

Significant variation in decision making for ICM patients:

Variation in medical care is a term used when patients with similar illnesses receive different treatments, and may be partly due to variable decision making. Data show that variation in decision making is mostly accounted for by the willingness and ability of physicians to offer management options rather than differences in illness or patient preferences[6]. This variation may be due to insufficiency of evidence supporting management strategies, problems in dissemination of evidence, variable interpretation of evidence, conflicts in available evidence, resistance to change, or bias resulting from anecdotal experience. This will result in apparent unwarranted randomness, instead of human wisdom, determining patients' management strategy. Therefore, identifying and reducing these variations must be a priority for any healthcare system. Great efforts have been made, for example in United States[7] and United Kingdom[8], to document glaring variations in providing medical care.

As shown in Table 2, individual physicians' practice patterns for the management of ICM patients vary widely, compared to LM patients. This variation may be due to several reasons. Conflicts in available evidence make physicians uncertain about the optimal management of ICM. More than 2 decades have passed since a meta-analysis of seven randomized trials, demonstrated a significant advantage of CABG over medical treatment, in reducing mortality of patients with CAD, specifically those with mild to moderate LV dysfunction[1]. Although several nonrandomized studies confirmed this survival benefit in patients with mild, moderate and severe LV dysfunction[2], results of STICH trial showed that, in patient with LVEF ≤35%, there is no significant difference between medical therapy and CABG with respect to death from any cause[3]. So controversy continues about the role of CABG in the management of ICM. Furthermore, controversy exists about the role of viability study in decision making for ICM patients[4,5], while data on safety and efficacy of PCI in ICM is rare[6,7]. All these controversies may contribute to the significant variation among physicians in decision making for patients with ICM.

Another area of uncertainty is management of ICM in certain subgroups such as elderly patients, patients with co morbidities (e.g. chronic kidney disease or severe obstructive lung disease) or patients with poor targets for revascularization. Efficacy of revascularization procedures in these subgroups has not been evaluated sufficiently, as they were usually excluded from trials. This may also result in variable management strategies among individual physicians.

Variation in decision making of different physicians not only reflects variable clinical practice of these physicians,

but might partly reflect heterogeneous demographic, clinical, echocardiographic and angiographic characteristics of patients visited by each physician. This seems unlikely to be the case in this study, as assignment of patients to different cardiologists at THC is usually a random process. Furthermore, the same consideration applies to LM group with still negligible variation in decision making.

Another area of concern, is that the ICM group as opposed to LM group, is more heterogeneous with regard to coronary anatomy and LV function. To ensure that this heterogeneity is not a significant cause of variation in decision making, we evaluated a more homogeneous subgroup of 294 patients with severe 3VD (>70% stenos is) and moderate LV dysfunction (30%≤LVEF<45%); variation of decision making even increased in this subgroup. The range and standard deviation for proportion of CABG recommendation, for example, increased from 31.1% and 8.9%, to 42.9% and 12.5%, respectively.

Several studies have demonstrated significant variation in utilization of cardiovascular procedures among different geographic regions[8], insurance programs[9], hospitals[10], or ethnic groups[11].In this study, we evaluated variation in decision making for a specific cardiovascular disease among different physicians, in a single university hospital. We believe that a multicenter study of community hospitals may show even greater variation in decision making. With significant variation in recommendations, concerns may rise about significant over or under-recommendation of procedures.

High rate of CABG non-adherence in ICM patients:

When CABG was recommended by caring cardiologist, ICM patients adhered to this recommendation less commonly than LM patients within 1 year from angiography (Figure 1 and 2).Under-recommendation by physicians and non-adherence by patients, both result in underuse of procedures.

Several studies have evaluated underuse of coronary revascularization procedures using appropriateness or necessity criteria. These studies have demonstrated that 21 to 34% of patients for whom revascularization, either CABG or PCI, is deemed appropriate or even necessary, do not receive any revascularizationat all[12-15]. In this study, we also determined that 32.4% of ICM patients and 10.0% of LM patients with CABG recommendation, did not receive this procedure within the specified period.

Predictors of CABG non-adherence:

We performed this part of study to scrutinize possible causes of high rate CABG non-adherence in ICM patients. It was demonstrated that advanced age, creatinine level >2$^{mg/dl}$, severe LV dysfunction, and moderate or severe mitral regurgitation are independent predictors of CABG non-adherence. In contrast, being married, presence of angina pectoris and moderate or severe left main disease are negatively correlated with it (Table 3).

Higher rate of CABG non-adherence among ICM patients may be due to several reasons. First, controversies about the optimal management of ICM, may indirectly lead to patient non-adherence. When symptom or survival benefit of procedures is not consistently shown by evidence, physicians less rigorously pursue adherence to these procedures. Furthermore, when patients consult with another cardiologist or cardiac surgeon, receiving a different recommendation makes them less confident with their physician's decision making, again leading to patient refusal. This is supported by the lower rate of CABG non-adherence among LM patients. Even among ICM patients, the more severe is the LM disease the less common is the CABG non-adherence (Table 3). Physicians consistently believe that CABG is the optimal management of LM disease, but this is not the case for ICM.

Second reason for the higher rate of non-adherence among ICM patients may be their worse risk profile for CABG, compared to LM patients. Therefore, they are less commonly selected for CABG by cardiac surgeons, despite cardiologist's recommendation. This is supported by the observed association of CABG non-adherence with advanced age, severe LV dysfunction, severe mitral regurgitation and serum creatinine more than 2$^{mg/dl}$, which are associated with increased operative risk.

While marital status isa patient related factor, most of the other predictors (i.e. LV function, mitral regurgitation, left main disease and creatinine level) are generally physician related. It means that to reduce underuse of CABG or probably any lifesaving procedure, most efforts should be focused on improving knowledge and practice of physicians involved in decision making for these patients. Obviously, this needs large scale well designed randomized trials to definitely clarify the role of these procedures in the management of ICM, as a whole or for certain subgroups.

Poor outcome of CABG non-adherence:

It was demonstrated in this study that for ICM patients with CABG recommendation, not performing CABG is associated with adverse clinical outcome. This association persisted after adjusting for confounding factors in Cox's proportional hazards model (Figure 3 and 4). Likewise, in previously mentioned studies about underuse of revascularization, it was shown that patients who are considered appropriate for revascularization, have adverse outcome if they do not receive the procedure[16-19].

Strengths and limitations:

This study was performed in a single university hospital. A multicenter study in community hospitals may reveal different results.

Some patients with CABG recommendation who have not received the procedure, may not really have had the chance of. Some of them might have died while they were in waiting lists, unfairly increasing rate of CABG non-adherence. It was not possible to exactly define the

proportion of such patients. In our setting, patients may remain in waiting list for up to one month; so this possibility seems negligible.

While more favorable outcome of patients with CABG is most probably due to symptom and survival benefits of CABG in ICM patients, several other considerations should be mentioned. First, some of patients who have died in CABG non-adherence arm, may have been critically ill or high risk patients who died in the same admission before scheduled CABG. This may unfairly increase mortality of non-adherence arm. To address this possibility, we excluded four patients who died within 5 days from angiography without revascularization[20-23]. Second, the better clinical outcome of patients undergoing CABG, may be partly due to selection bias. Patients with better risk profile are more commonly selected for CABG, resulting in better outcome. Although the same results were obtained after adjusting for confounding factors, the possibility of residual confounding should be considered. Third, the better outcome associated with a procedure, may not be all the result of procedure itself, but may be partly caused by better care coming with the procedure. Patients receiving CABG may have better compliance and more regular follow-up visits, leading to better clinical outcome.

Conclusions

Although ICM is an extremely common disorder encountered frequently in daily practice of any cardiologist, insufficient and conflicting evidence supporting its management has resulted in variable and individualized approach of cardiologists toward its management. This concept, along with higher risk profile of these patients, may have resulted in significant underuse of lifesaving procedures. Accordingly, large-scale well-designed trials on the management of ICMas well as improving knowledge and practice of physicians toward its management are warranted.

Conflict of Interest: The authors declare no conflicts of interests

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