Assessment of Effect of Diabetes on Health-Related Quality of Life in Patients with Coronary Artery Disease Using the EQ-5D Questionnaire

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ABSTRACT

Objective: To assess the influence of diabetes on health-related quality of life (HRQOL) in patients with coronary artery disease (CAD) and identify predictors of health status at 1-year follow-up after an acute coronary event. Methods: A prospective cohort study in patients diagnosed with CAD at a tertiary care hospital from India. The EuroQol five-dimensional (EQ-5D) questionnaire was administered at 1-year follow-up. Multivariate stepwise linear regression was used to assess predictors of EQ visual analogue scale (VAS) and EQ-5D questionnaire utility scores. Respondents reporting problems on the EQ-5D questionnaire were stratified by the presence of diabetes at baseline for comparison. Results: Of 960 (30% diabetic) patients with CAD enrolled in a main study cohort, 306 (76% males, 21% diabetic) responded to the HRQOL questionnaire at 1 year. Diabetic patients reported more difficulties/problems than did non-diabetic patients for EQ-5D questionnaire dimensions (mobility, 12.3% vs. 4.1%, \( P = 0.03 \); usual activities, 56.9% vs. 41.3%, \( P = 0.03 \); pain/discomfort, 50.8% vs. 17.8%, \( P < 0.001 \); anxiety/depression, 33.8% vs. 14.9%, \( P < 0.001 \), except for self-care (12.3% vs. 17.5%, \( P = 0.35 \)). Mean ± SD EQ VAS and EQ-5D questionnaire utility scores were significantly lower for patients with CAD with diabetes versus those without diabetes (0.75 ± 0.15 vs. 0.83 ± 0.15, \( P = 0.0002 \), and 67.8 ± 8.8 vs. 73.6 ± 5.4, \( P = 0.0001 \), respectively). Presence of diabetes, use of beta-blockers on discharge, and treatment strategy significantly influenced the VAS score, whereas myocardial infarction as final diagnosis and the presence of prior CHF predicted worse EQ-5D questionnaire utility scores. Conclusions: The poorer HRQOL as assessed by the EQ-5D questionnaire among patients with CAD who had diabetes highlights the need of individualized treatment programs to improve outcomes in this most vulnerable population. Keywords: coronary artery disease, diabetes, EQ-5D, health-related quality of life.

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Introduction

Coronary artery disease (CAD) remains a leading cause of mortality and morbidity in India and worldwide [1]. During recent decades, the prevalence of CAD in India has progressively increased with an estimated adult prevalence of around 11% in urban settings and 5% in rural areas [2]. CAD imposes a considerable economic loss. For Indian population, the number of productive years of life lost due to CAD is projected to increase nearly twofold by 2030 since 2004 [3].

Morbidity and mortality in patients with CAD has improved to a great extent because of advances in treatment landscape [4]. Conventional treatments for CAD mainly focus on clinical outcomes, such as survival and extending life. The increased survival of patients with CAD along with the considerable physical, emotional, and social consequences for survivors demand that assessment of health-related quality of life (HRQOL) is critical to measure clinical outcomes and effectiveness of health care and evaluate the overall well-being of the patients [5]. There has been a significant development in the measurement of quality of life as an indicator of health outcomes in patients with CAD. The burden of CAD can be significant; reducing frequency and severity of the disease as well as improving physical functioning remain significant determinants of overall HRQOL in patients with CAD [5].

Diabetes is an established and highly prevalent risk factor for cardiac morbidity and mortality that worsen prognosis in patients with CAD [6–8]. Despite optimal management, it is difficult to improve well-being in diabetic patients and outcomes for patients with CAD and diabetes remain poor [9]. Limited studies have examined the factors associated with health status outcomes after CAD. Little is known about risk factors that influence patient-reported outcomes among patients with CAD from India. In this study, therefore, we aimed to compare HRQOL in patients with CAD with or without diabetes and identify predictors of health status at 1 year after an acute CAD event.

Conflicts of interest: The authors have indicated that they have no conflicts of interest with regard to the content of this article.

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http://dx.doi.org/10.1016/j.vhri.2014.02.004
Methods

Study Design
This was a prospective observational study conducted between January 2011 and January 2012 at a tertiary care hospital from Jaipur (India). The detailed study design is reported elsewhere along with the main study cohort results [10].

Inclusion Criteria
Consecutive patients of both genders, aged 18 years or older, hospitalized at the cardiac intensive care unit of a tertiary care hospital were considered. Patients who underwent coronary angiography and diagnosed with myocardial infarction (MI), unstable angina, or chronic stable angina on final diagnosis were considered to have CAD using standard definitions [11]. Patients were identified as a known case of CAD on the basis of at least one of the following criteria: history of documented angina/infarction, electrocardiogram findings suggestive of silent MI, a positive treadmill test result or stress echocardiography highly suggestive of silent MI, history of angina/MI with electrocardiogram confirmation, angiographic evidence of CAD, or history of percutaneous transluminal coronary angioplasty/coronary artery bypass grafting (CABG). Patients were identified as diabetics if they met any of the following criteria: at least one prescription of antidiabetic drug (as verified by clinical records), ongoing antidiabetic treatment (with or without prescription), or elevated hemoglobin A1C level (hemoglobin A1C ≥ 7). Patients with a history of hypertension and/or on treatment for hypertension or having at least two elevated blood pressure measurements were considered hypertensive.

Exclusion Criteria
Patients who did not undergo coronary angiography or diagnosed with normal coronary artery after coronary angiography and/or atypical chest pain were excluded.

Procedures
Discharge summaries of patients were reviewed to collect demographic information, vital signs, and details of other risk factors for CAD such as presence of diabetes, hypertension, and history of CAD. Information pertaining to treatment strategies (medical management, percutaneous transluminal coronary angioplasty, or CABG) and medications prescribed at discharge was collected. Patients were followed-up via telephonic interview at 1 year after an acute CAD event and the EQ-5D questionnaire—a standardized generic instrument—was administered to assess HRQOL. The EQ-5D questionnaire comprises the EQ-5D questionnaire descriptive system and a visual analogue scale—the EQ VAS [12,13].

The descriptive system comprises five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression, with each dimension having three levels of perceived problems: no problems (level 1), some problems (level 2), and extreme problems (level 3). For EQ VAS, respondents can indicate their overall self-rated health state on a scale ranging from 0 to 100, where 0 is equivalent to the “worst imaginable health state” and 100 is equivalent to the “best imaginable health state.” Together, the descriptive system and the EQ VAS give valuable information on the health states of individuals, groups of patients, and populations. An overall utility score (EQ-5D questionnaire utility score) was also calculated on the basis of these dimensions, with the score ranging from 0, representing states as bad as being death, to a maximum of 1, representing full health.

For our study, EQ-5D questionnaire utility scores were derived on the basis of the UK population because it can be applied to other populations when country-specific weights are not available [14], as in the case of India.

Statistical Analyses
All data entries and analyses were performed using Statistical Package for Social Sciences (SPSS, version 17.0; SPSS, Inc., Chicago, IL). The respondents were stratified into two groups by presence of diabetes at baseline. Data obtained from the EQ-5D questionnaire descriptive system were reported as frequencies and percentages of respondents having particular levels in particular dimensions. The frequencies of reported level 3 problems in this study were very low (<2% of total respondents), so it was more convenient to dichotomize the EQ-5D questionnaire levels into “no problems” (level 1) and “any problem” (levels 2 and 3), thereby changing the profile into frequencies of reported problems [15]. The chi-square test was then applied to test differences in reported problems between diabetic and nondiabetic patients with CAD. An independent t test was used to detect differences between the mean ± SD of EQ VAS scores for patients with CAD with or without diabetes.

EQ-5D questionnaire utility scores for patients with CAD with or without diabetes were compared using an independent t test. The multivariate stepwise linear regression models were used to assess predictors of the EQ VAS and EQ-5D questionnaire utility scores. The independent variables studied include age, presence of hypertension, diabetes, congestive heart failure (CHF), sex, prior MI, final diagnosis, final treatment, and use of key evidence-based medication at discharge.

Odds ratios (ORs; 95% confidence intervals, 95% CIs) for reporting problems in all the five EQ-5D questionnaire dimensions were calculated using binary regression in patients with or without diabetes at baseline to quantify the effect of diabetes. P < 0.05 was considered statistically significant, whereas P < 0.001 was considered statistically highly significant.

Results
Of 960 patients with CAD enrolled in the cohort study, 306 (231 [76%] males; 65 [21%] diabetic patients) patients responded to the HRQOL questionnaire at 1-year follow-up after an acute CAD event.

Baseline Demographic and Clinical Characteristics
Baseline demographic characteristics, clinical characteristics, and angiography findings of all the respondents (stratified by the presence of diabetes) are presented in Table 1. Patients who had diabetes at baseline were older, had 2 times higher proportion of hypertension, and also a higher proportion of unstable angina on final diagnosis.

**EQ-5D Questionnaire Assessments**
Findings from assessment of each of the five dimensions of the EQ-5D questionnaire are given in Table 2. Diabetic patients were likely to experience more difficulties or problems compared with nondiabetic patients for all the EQ-5D questionnaire dimensions, except self-care. A significantly higher proportion of diabetic patients (vs. nondiabetic patients) reported pain or discomfort (50.8% vs. 17.8%) as well as anxiety or depression (33.8% vs. 14.9%) (P < 0.001 in each case).
At 1-year follow-up, both mean (± SD) EQ VAS and EQ-5D questionnaire utility scores were significantly lower for patients with CAD who had diabetes versus those who did not have diabetes (67.8 ± 8.8 vs. 73.6 ± 5.4, P = 0.0001, and 0.75 ± 0.15 vs. 0.83 ± 0.15, P = 0.0002, respectively) (Fig. 1).

Table 3 shows findings of the multivariate stepwise linear regression models used to assess the influence of various risk factors on 1-year EQ VAS and EQ-5D questionnaire utility scores. The presence of diabetes showed statistically highly significant negative correlation (P < 0.001) with 1-year EQ VAS and EQ-5D questionnaire utility scores. The use of beta-blockers on discharge and final treatment significantly influenced the EQ VAS score (P < 0.05 in each case), whereas MI as final diagnosis and presence of prior CHF were associated with worse EQ-5D questionnaire utility scores at 1 year.

Binary regression models demonstrated that the presence of diabetes at baseline was associated with reporting of more difficulties in patients with CAD at 1-year follow-up for all EQ-5D questionnaire dimensions, except self-care (mobility: OR 6.5 [95% CI 2.1–20.0]; usual activities: OR 1.9 [95% CI 1.1–3.2]; pain/discomfort: OR = 4.8 [95% CI 2.7–8.6]; anxiety/depression: OR 3.1 [95% CI 1.6–5.9]).

Discussion

In recent years, more emphasis has been given to patient-reported outcome measures such as HRQOL and health utility within the cardiovascular field [16]. HRQOL is defined as patients’ subjective evaluations of influences of their current health status, health care, and health-promoting activities on their ability to achieve and maintain a level of overall functioning that allows them to pursue valued life goals and that is reflected in their general well-being [5]. Because of the inherent nature of the disease, patients with CAD are known to perceive poorer quality of life than do patients without CAD [17,18]. It has been observed that heterogeneity among individuals’ characteristics such as varied comorbid conditions and the environment (e.g., different countries) also influence the HRQOL [19]. Overall, predictors of HRQOL can be grouped into physiological/biological factors (e.g., prior cardiovascular events, CHF, and diabetes), symptoms (emotional and cognitive variables such as depression and anxiety), individual characteristics (e.g., age and sex), and environmental characteristics (e.g., optimization of medical treatment and cardiac rehabilitation programs) [20].

The goal of the present study was to examine the association between diabetes and patients’ health status outcomes at 1 year after an acute event among patients with CAD. Our results illustrated that patients with CAD and coexisting diabetes had a significantly higher prevalence of hypertension, more likely to present with unstable angina, and were more likely to undergo CABG after hospitalization. It is expected that HRQOL is considerably affected in patients after a cardiac event, especially during the initial recovery phase. Even though improvement in HRQOL occurs over time, the persistence of residual distress at 1-year follow-up remains a challenge for clinicians concerned with full rehabilitation of the cardiac patient [21,22]. Therefore, the measurement of HRQOL and the assessment of factors affecting the quality of life may help to improve and sustain the improved quality of life in patients with CAD.

Diabetes has been established as an important comorbidity in patients with CAD. Our study results at 1-year follow-up after an acute coronary event revealed that patients with CAD with
diabetes reported more difficulties or problems in mobility, usual activities, comfort, and mental health status than did patients with CAD who did not have diabetes at baseline. It is known that patients with diabetes often have a high burden of coronary atherosclerosis [23], resulting in severe CAD. Hence, it is not surprising that at 1 year after an acute event, patients with diabetes were more likely to have a negative influence on health status outcomes as observed in our study. Similar findings have also been reported by earlier studies [24–26]. The prospective cohort study by Peterson et al. [24] evaluated the influence of diabetes on patients’ health condition 1 year after an acute attack in patients with acute coronary syndrome (ACS). The findings of this study demonstrated that patients with diabetes are considerably more likely to experience angina, cardiac-specific physical limitations, and worse HRQOL results 1 year after ACS than do nondiabetic patients. The results from our study enrich current scientific knowledge as well as confirm the negative impact of diabetes on HRQOL in the Indian population as well after discharge. The data from recent studies among patients with CAD from India have demonstrated opportunities for improving post-ACS care [27,28]. Similarly, results from our study also support the need for an early identification and aggressive treatment of diabetes in patients with CAD to improve long-term outcomes. Given the expected adverse outcomes in high-risk patient population, clinicians should be more sensitive to potential influences of concomitant comorbidities, such as diabetes, on health outcomes. One of the many possible alternative approaches to improve postdischarge outcomes among patients with CAD with diabetes could be using customized strategies to enhance postdischarge surveillance by patient awareness programs such as disease management or cardiac rehabilitation [9,29]. This is imperative from local clinical practice perspective taking into consideration the fact that the prevalence of diabetes in India (particularly among patients with CAD) remains considerably high (studies have reported the prevalence of diabetes at around 40% [27,28,30], and it is also increasing rapidly).

**Table 3 – Predictors of EQ VAS and EQ-5D questionnaire utility scores at 1- y follow-up.**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Partial regression coefficient</th>
<th>SE</th>
<th>Standardized partial regression coefficient</th>
<th>t</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dependent variable: EQ VAS score</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>-6.271</td>
<td>0.865</td>
<td>-0.385</td>
<td>-7.245</td>
<td>0.000</td>
</tr>
<tr>
<td>Discharge medication, beta-blocker</td>
<td>-2.021</td>
<td>0.712</td>
<td>-0.150</td>
<td>-2.836</td>
<td>0.005</td>
</tr>
<tr>
<td>Final treatment</td>
<td>1.390</td>
<td>0.500</td>
<td>0.148</td>
<td>2.779</td>
<td>0.006</td>
</tr>
<tr>
<td>Dependent variable: EQ-5D questionnaire utility score†</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>-0.085</td>
<td>0.020</td>
<td>-0.229</td>
<td>-4.207</td>
<td>0.000</td>
</tr>
<tr>
<td>Final diagnosis</td>
<td>-0.051</td>
<td>0.014</td>
<td>-0.196</td>
<td>-3.496</td>
<td>0.001</td>
</tr>
<tr>
<td>CHF</td>
<td>-0.058</td>
<td>0.019</td>
<td>-0.171</td>
<td>-3.046</td>
<td>0.003</td>
</tr>
</tbody>
</table>

Independent parameters studied: age (< 45 vs. ≥ 45 y), hypertension (present vs. absent), diabetes (present vs. absent), CHF (history of heart failure or ejection fraction ≤ 40%; present vs. absent), sex (male vs. female), prior MI (present vs. absent), final diagnosis (unstable angina or MI) and final treatment (medical management vs. PTCA or CABG), and use of key evidence-based medication (antiplatelet agent, beta-blocker, antihyperlipidemic agent, and ACEI/ARB).

ACEI/ARB, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers; CABG, coronary artery bypass grafting; CAD, coronary artery disease; CHF, congestive heart failure; EQ-5D, EuroQol five-dimensional; MI, myocardial infarction; PTCA, percutaneous transluminal coronary angioplasty; VAS, visual analogue scale.

* R = 0.41, R² = 0.17, adjusted R² = 0.16, F = 20.06, P < 0.001.
† R = 0.32, R² = 0.10, adjusted R² = 0.09, F = 11.57, P < 0.001.
Another important finding of our study was the negative association of diabetes with both VAS scores and EQ-5D questionnaire utility scores in patients with CAD than in their non-diabetic counterparts. The model assessing predictors of the VAS score implicates that diabetes along with the appropriate use of beta-blockers at discharge and treatment strategy (medical management vs. interventional or surgical) remain crucial for favorable health outcomes. There are inconsistencies among findings of studies assessing the influence of diabetes on patients’ health condition as per treatment strategy after an event. Kim et al. [31] have demonstrated that patients who undergo an early invasive strategy (percutaneous coronary intervention) show better life quality results than do patients treated with the traditional method, whereas other studies have shown no difference in life quality between the percutaneous coronary intervention and the CABG group compared with medical management [32,33]. Simpson and Pilote have demonstrated no connection between diabetes and life quality in patients with ACS [34]. A recent study by Kim et al. [35] has proposed the need of comprehensive supportive care to improve the general health status of ACS survivors and improve long-term clinical outcomes [35]. In a model predicting factors influencing EQ-5D questionnaire utility scores, final diagnosis and prior CHF along with diabetes contributed significantly. Because it is not possible to revert the final diagnosis neither change the history of CHF, this finding indicates a need of more aggressive treatment plan for diabetes in patients with CAD after an acute event to improve outcomes—especially if an individual is a known case of heart failure. In the absence of country-specific utility references for the Indian population, the EQ-5D questionnaire utility scores from our study may provide a preference-based score for future cost-effectiveness analyses until the country reference value set is developed.

Limitations
While interpreting the results of this study, certain limitations have to be taken into consideration. First, because of the observational study design, no information regarding missing data can be provided. The diagnosis of diabetes was based on the review of medical records alone; no information was available about diabetes duration or adequacy of control, and patients with undiagnosed diabetes may have been misclassified. The observation on HRQOL assessments were made at 1-year follow-up as the full recovery, including the ability to perform daily activities, can be made within this period after hospitalization. For this reason, results of this study are preliminary and call for another study assessing long-term outcomes with a larger patient population. Last, although most of the known risk factors were considered in models assessing predictors for EQ VAS and EQ-5D questionnaire utility scores, the small values of adjusted R² warrant further exploratory studies to ascertain other possible risk factors.

Conclusions
To our knowledge, this is the first study assessing the influence of diabetes on HRQOL among patients with CAD from India. The study confirmed that diabetes remains a critical predictor of health outcomes among patients with CAD. The poorer HRQOL in diabetic patients with CAD underline the need of individualized treatment programs to improve outcomes in this most vulnerable subgroup of CAD population.

Acknowledgment
We thank Dr. Ashok Jain, senior cardiologist, Narayana Hrudayalaya Hospital, Jaipur, for extending his cooperation to accomplish data collection.

Source of financial support: The authors have no financial relationships to disclose.

References


