Gender and Diabetes Mellitus Relevance on Outcomes of Coronary Artery Bypass Grafting. A Retrospective Study

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Abstract

Purpose: For the group of patients with coronary artery disease (CAD), referred to coronary artery bypass surgery, we sought to asses the relevance of gender and presence of Diabetes Mellitus upon survival rates, within the first 3 years after surgery. *Methods*: At "Nicolae Stancioiu" Heart Institute, a number of 110 patients were followed up from September 2003 to February 2008, for the following events: ischemia, restenosis, atrial fibrillation, ventricular arrhythmias, heart failure, other events and complications. Ages, gender, presence of Diabetes Mellitus were noted. For the diabetic/non-diabetic (45 diabetic, 65 non-diabetic) groups and male/female groups (27 female, 83 male), we applied in the SPSS program the Logrank and Wilcoxon tests, for quantifying the differences in the survival rates between the groups. *Results*: No significant differences were found in the survival rates between the groups (diabetic/non-diabetic Logrank test, p=0.71, Wilcoxon test, p=0.86; female/male Logrank test, p=0.7, Wilcoxon test, p=0.95). Also for the subgroup of patients which had in-graft restenosis (46 patients) no significant differences were found between the diabetic/non-diabetic (Logrank test, p=0.36) and gender groups (Logrank test, p=0.4). Mean age for the whole group is 59.2 (61.9 for female and 58.3 for male). *Conclusion*: Diabetes Mellitus or sex is not significant factors for lower survival rates, in the first 3 years after coronary artery bypass.

Keywords: Coronary bypass; Diabetes; Survival rate.

Introduction

Patients remain at high risk of subsequent major cardiovascular events after coronary artery bypass grafting (CABG) [1]. For long term outcomes, diabetes is well documented to be a prognosis factor for increased rates of mortality, following CABG [2]. The issue of whether gender is a risk factor for long term mortality after interventions is still controversial [3]. Secondary prevention may have to be focused on more comprehensive risk factor modifications to bring patients to target goals [1]. For the particular case of restenosis, also there is documented evidence that failing to reduce the risk factors for atherosclerosis will eventually (in the next 25 years) lead to reintervention for more than 50% of the patients [4].

With the necessity of following the patients with coronary artery disease (CAD) for their entire life, local particularities in clinical post-surgery outcomes are important. A study in a local center from Romania, "Nicolae Stancioiu" Heart Institute from Cluj-Napoca, appears essential for establishing risk factors for higher morbidity that might be regional, and their implications, and thus to improve their pre- and post-operative management, by the entire health system, with final goal in reducing overall death-rates and medical costs. A study assessing relevance of gender or diabetes on mid and long term outcomes is thus relevant.

Material and Method

From the group of patients that were referred for CABG, at Cluj-Napoca Heart Institute, we selected the 110 cases that returned for hospitalization, from September 2003 to February 2008. The patients were divided into 4 groups: diabetic/non-diabetic and females/males. The noted events that lead for rehospitalisation were: ischemia, restenosis, atrial fibrillation, ventricular arrhythmias, heart failure, other events and complications (post-operative for ex.). The distinction of ischemia from restenosis is necessary as other vessels than the bypassed ones might become stenosed.

For the 4 groups of patients, 45 diabetic- 65 non-diabetics, and 27 female- 83 male, we compared the survival rates within the first 36 months from surgery, using Kaplan-Meyer method and Logrank and Wilcoxon tests. Statistics were calculated with SPSS statistical software.

Mean age for the whole group was of 59.2 (61.9 for female and 58.3 for male).

Results

Of the 110 patients, 8 were censored from further calculations due to having one ore more complications, after the 36 months time-limit. From the initial group of 102, 46 patients had ingraft restenosis, thus resulting that resteonsis remains the most common complication for bypassed patients.

In both the female/male and diabetic/non-diabetic groups no significant statistical differences were found in the survival rates (Table 1). Survival diagrams also show no particular elapse between the groups (Figures 1 and 2).

Compared groups	Logrank (p-value)	Wilcoxon (p-value)
Female (n = 27)/male (n = 83)	0.71	0.14
Diabetic $(n = 45)/non-diabetic (n = 65)$	0.7	0.14

Table 1. "p" values for the compared groups

For the subgroup of patients that had restenosis, also diabetes or gender had no significant influence (Table 2).

Table 2. Statistical significance (p-value) for the compared groups: in case of restenosis

Sub-group	Logrank (p-value)	Wilcoxon (p-value)
Female $(n=9)/Male (n=37)$	0.40	0.81
Diabetic $(n=20)$ /Non-diabetic $(n=26)$	0.36	0.85

Survival Functions

Figure 1. Survival diagrams for diabetic/non-diabetic groups



Survival Functions

Figure 2. Survival diagrams for female/male groups

Discussion

For the female vs. male groups, the results that we obtained appear to concord with data published in literature. Koch A.G. et al., conclude in 2003 that disease prevalence in women, and not gender per se, affects mid- and long-term survival after cardiac surgery [5]. In a retrospective

study with a group of 1758 patients, Sharoni E. concludes in 2009 that the female patients had significantly higher postoperative mortality (p < 0.05), but, that strong predictors of death were cardiopulmonary bypass time, use of an intra-aortic balloon pump, and, to a lesser extent, chronic obstructive pulmonary disease and thus female gender was not found to be an independent risk factor for death [6]. More, Ennker I.C. publishes data to support that female sex per se does not increase operative risk, but shorter height, which is more common in women, affects the outcome, probably due to technical difficulties in shorter patients with smaller internal mammary arteries and coronary vessels [3].

From other points of view, there are studies to support that female gender is at higher risk of complication. Deaton C. states that both diabetes and female sex are predictors for worse outcomes, in first three months after surgery [7]. Emmert M.Y. finds by multivariate analysis that in case of off-pomp CABG, women have worse outcomes, primarily due to longer intensive care required, and higher stroke rate [8]. Mack M.J. finds in a group of 4336 patients that there were no differences in outcomes between on-pump and off-pump CABG [9].

It should be added here, that in a 1-year outcome study, Mehta R.H. states that in a group of 13 207 patients which underwent CABG, males were more unlikely to achieve variable risk-factors reduction [1]. This data is supporting the need for further research for genetic differences [8], as male patients seem to have at least same outcome post CABG, in spite of the lack of risk-factor control.

Our findings are that the women group did not have a worse outcome. The variables weren't correlated with other variables such as other diseases, pre-operatory conditions or height. One explanation could be that doctors, both surgeons and anesthesiologists take into account individual differences, and manage special situations as well in both groups (such as size of arterial graft, or intra or post surgical emergencies). Other explanation could be that the male group actually had a worse outcome, in terms of survival rates, due to life-style and risk factors lack of correction.

Further studies are necessary to be conducted, in order to establish and correlate other possible factors.

For the survival rates compared between the diabetic/non-diabetic groups our findings are supported by a part of literature. Kim W.J. states from a 690 study group of patients with CABG, that the prognostic impact of diabetes on long-term treatment with DES or CABG for patients with unprotected LMCA (left main coronary artery) disease was minimal [10]. Qiang J. finds in a group of 140 patients, all over 65 and diabetic (31% of the population of the study), that they shared almost similar rates among other morbidities and mortality as compared to non-diabetic patients over 65 years of age [11]. Furthermore, Schmeltz L.R. states concerning an improved insulin-preoperative management for insulin-dependent cases, that on multivariate analysis, a preoperative diagnosis of diabetes was not a significant factor in postoperative mortality or pulmonary complications. In CABG-only patients, no significant differences were seen in outcomes between diabetic and non-diabetic patients [12].

For the patients with LV (left ventricular) dysfunction, Wang W. finds that diabetes is not a predictor for mortality, but is a predictor for co-morbidities and rehospitalisation [13]. For a long-term of 6 years, Mohammadi S. publishes a study including 735 insulin-dependent diabetic patients that non-insulin-dependent diabetes is not a predictor for worse outcome, but insulin-dependent diabetes is [14]. At a 5 year follow up, Kunadian B. states diabetes as worse outcome predictor, in the particular case of using cross clamp fibrillation method [15].

Bigger studies clearly demonstrate that on long term, diabetes is a predictive factor, concerning us for the entire life risk-management of CAD patients. Sabik J.F. concludes in a study with 48 758 patients followed for 25 years, that at 15 years post-surgery, 27% had reinterventions. Diabetes was a predictive factor, but there were no differences between the oral treatment and insulin treated groups. Only diabetic subgroup of patients that had a lower rate of complications was the dietcontrolled diabetic group). At 5 years reintervention was present at 4% of the patients [4].

One explanation for the data we obtained might be that the 3-year exclusion criteria is too short, and in longer time, rehospitalisation, especially for the same occluded artery, is to be expected more often in diabetic patients. Though not significant for CABG outcomes, the diabetic population in our study was 41%.

Study limitations. There are a series of limitations in our study. First, the type of stable/unstable CAD was not noted, and might have been important in the relevance of diabetes upon mid term survival rates. Secondly, it would have been relevant to separate the short time complications from other. Type of diabetes (insulin vs. non-insulin dependent) might have been important.

Multivariable tests were not conducted, to compare the groups by terms of pre-operatory co morbidities.

Conclusion

For the patients undergoing CABG, gender and diabetes are not predictors for lower survival rates, within the first 3 years after surgery, but other studies are needed, for longer periods of time, and including other variables, in order to confirm which other predictors lead to this conclusion.

Ethical Issues

This retrospective research is in accordance with all ethical standards.

Conflict of Interest

The authors declare that they have no conflict of interest.

References

- 1. Mehta RH, Bhatt DL, Steg PG, Goto S, Hirsch AT, Liau CS, et al. Modifiable risk factors control and its relationship with 1 year outcomes after coronary artery bypass surgery: insights from the REACH registry. Eur Heart J 2008;29(24):3052-60.
- Kajimoto K, Kasai T, Miyauchi K, Hirose H, Yanagisawa N, Yamamoto T et al. Metabolic syndrome predicts 10-year mortality in non-diabetic patients following coronary artery bypass surgery. Circ J 2008;72(9):1481-6.
- 3. Ennker IC, Albert A, Pietrowski D, Bauer K, Ennker J, Florath I. Impact of gender on outcome after coronary artery bypass surgery. Asian Cardiovasc Thorac Ann 2009;17(3):253-8.
- 4. Sabik JF 3rd, Blackstone EH, Gillinov AM, Smedira NG, Lytle BW. Occurrence and risk factors for reintervention after coronary artery bypass grafting. Circulation 2006;114(1 Suppl):1454-60.
- Koch CG, Weng YS, Zhou SX, Savino JS, Mathew JP, Hsu PH et al. Prevalence of risk factors and not gender per se, determines short- and long-term survival after coronary artery bypass surgery. J Cardiothorac Vasc Anesth 2003;17(5):585-93.
- 6. Sharoni E, Kogan A, Medalion B, Stamler A, Snir E, Porat E. Is gender an independent risk factor for coronary bypass grafting? Thorac Cardiovasc Surg 2009;57(4):204-8.
- Deaton C, Thourani V. Patients with type 2 diabetes undergoing coronary artery bypass graft surgery: predictors of outcomes. Eur J Cardiovasc Nurs. 2009 Mar;8(1):48-56. Epub 2008 Jun 3.
- Emmert MY, Salzberg SP, Seifert B, Schurr UP, Odavic D, Reuthebuch O, Genoni M. Despite modern off-pump coronary artery bypass grafting women fare worse than men. Interact Cardiovasc Thorac Surg 2010;10(5):737-41.
- Mack MJ, Prince SL, Herbert M, Brown PP, Katz M, Palmer G et al.. Current clinical outcomes of percutaneous coronary intervention and coronary artery bypass grafting. Ann Thorac Surg 2008;86(2):496-503
- 10. Kim WJ, Park DW, Yun SC, Lee JY, Lee SW, Kim YH et al. Impact of diabetes mellitus on the treatment effect of percutaneous or surgical revascularization for patients with unprotected left

main coronary artery disease: a subgroup analysis of the MAIN-COMPARE study. JACC Cardiovasc Interv 2009;2(10):956-63.

- 11. Qiang Ji, Yunqing Mei, Xisheng Wang, Jing Feng, Jiangzhi Cai, Yifeng Sun. Impact of Diabetes Mellitus on old patients undergoing coronary artery bypass grafting. International Heart Journal 2009;50:693-700.
- 12. Schmeltz LR, DeSantis AJ, Thiyagarajan V, Schmidt K, O'Shea-Mahler E, Johnson D et al. Reduction of surgical mortality and morbidity in diabetic patients undergoing cardiac surgery with a combined intravenous and subcutaneous insulin glucose management strategy. Diabetes Care 2007;30(4):823-8.
- 13. Whang W, Bigger JT Jr. Diabetes and outcomes of coronary artery bypass graft surgery in patients with severe left ventricular dysfunction: results from The CABG Patch Trial database. J Am Coll Cardiol 2000;36(4):1166-72.
- 14. Mohammadi S, Dagenais F, Mathieu P, Kingma JG, Doyle D, Lopez Set al. Long-term impact of diabetes and its comorbidities in patients undergoing isolated primary coronary artery bypass graft surgery. Circulation 2007;116(11 Suppl):I220-5.
- 15. Kunadian B, Dunning J, Millner RW. Modifiable risk factors remain significant causes of medium term mortality after first time Coronary artery bypass grafting. J Cardiothorac Surg 2007;2:51.
- 16. Rosner B. Fundamentals of Biostatistics, Duxbury Press, Washington, 1995.