

# **Risk Factors associated with diabetic patients admitted to cardiology; A detailed overview**

## **Abstract**

The diabetic patients are at increased risk of cardiac failure. There are certain risk factors associated with patients of diabetes. The history of acute coronary syndrome (ACS) in patients of diabetes increases the risk of death from CV cause. Therefore, when compared with non-diabetic patients, cardiovascular diseases seem to be the pertinent cause of death in diabetic patients accounts to 30% to 40% of patients. The risk factors include LDL-cholesterol, age, gender, the left ventricular function, obesity, peripheral arterial disease or others are significant predictors of diabetic patients in cardiology wards. There are certain management strategies for patients of diabetes align with identification and targeting patients' CV risk factors. The cardiac structure and function are also altered by the insulin resistance and glycemic dysregulation with subtle modifications as an individual and specific factor for cardiac failure. Furthermore, patients of stress hyperglycemia during surgery or stay in ICU have negative outcomes as compared to those with prior diabetic history. The technique of literature review with the subsequent sections to discuss results and findings of the research aided with discussion is the selected procedure. The risk factors associated with diabetic patients admitted to cardiology are varied and significantly influences the patients' health with an increased risk of death due to cardiovascular diseases.

## **Introduction**

The patients with Diabetes Mellitus (DM) are at elevated risk of adverse events associated with cardiovascular disease. There are risk factors associated with the patients admitted to cardiology with the history of DM. The research study by Baluja et al, 2020 aims to assess several factors employing a risk model for action- based evaluation of the incidence of cardiac event in diabetic patient following ACS. It is reported in the study that history of ACS in patients are at an increased risk of death from CV causes and the patients with diabetes are at elevated risk of death following ACS opposed to non-diabetic patients. (Savonitto *et al.*, 2018) is of the view that after an ACS, CV events indicate 70% of all causes of death. The study by Baluja et al also reports that in acute myocardial infraction study for LVEF, the DM presence reveal a 37% high risk of mortality.

The second study by Breuker et al, 2018 restates the fact that cardiovascular diseases are the major cause of death in patients with diabetes. The study considers LDL-cholesterol as a risk factor and the assessment of LDL-C in diabetic patients increased cardiovascular risk while treated with statins. The study reports that adults with DM are at high risk of death from heart disease as compared to those without DM. LDL-C is considered to be a significant risk factor for CVD because of its role in the development of atherosclerosis (Gulati and Merz, 2016).

Budoff et al, 2016 reports that the increase in diabetic patients across the United States is associated with increased cardiovascular morbidity. The management strategies for diabetes are in line with identifying and targeting patients cardiovascular risk factors. This research refers to the previous research by Haffner et al which revealed that people with diabetes without myocardial infraction

(MI) had an increased risk of CHD as compared to those with MI supported by the study of (Malik *et al.*, 2011).

As per the study of Ernande, et al 2017 that resistance to insulin and glycemic dysregulation are the causes of elusive and progressive modifications in heart. Furthermore, type 2 diabetes mellitus (T2DM) acts as a specific and individualized factor for heart failure (HF) (Baeza-Román *et al.*, 2017). It can induce a diabetic cardiomyopathy and patients with T2DM the early cardiac modifications include *LV hypertrophy* and others as reported in the study (Ernande, et al 2017).

Galindo et al, 2018 is of the view that up to 40% patients undergoing cardiac surgery have a history of diabetes. Non-diabetic patients almost 60% develop stress hyperglycemia. It is reported in the study that perioperative hyperglycemia in diabetic patients increases risk of wounds, renal failure, length of hospital stays and others. The article by Galindo et al, 2018 discusses the strategies for the administration of hyperglycemia and diabetes in cardiac surgery patients.

## Literature Review

As per the study of Baluja et al, the participants in the study 55.9% of them were diagnosed with one major cardiac event (417 deaths). The model used in the study was Fine-Gray models and it shows that the 'PG-HACKER' risk factors which includes gender, age, peripheral arterial diseases and other factors listed at the first page of the article in the results section were associated with adverse cardiac events. In the discussion section of the article there is an overview of the major adverse cerebrovascular event (MACCE) in the diabetes population following ACS. It is reported in the study that patients of diabetes with prior ACS are more susceptible to have MACCE events as opposed to any other cause leading to patients' mortality.

The study proposes a scoring method that is simple and effective and it is PG-HACKER. This score is used to predict MACCE in diabetic patients. The worse outcomes related to a reduction in LVEF in the diabetic patients as shown in PG-HACKER risk score and left ventricular function is an important indicator and significant contributor to the research outcomes. Heart failure and death are associated with DM without any significant role of LVEF. There are benefits of PG-HACKER score and it is designed with an aim to increase awareness for patients and provider alike. It is an important point of discussion that a clinical practice for high risk ACS has the certain objective and that is to improve long term prognosis with an aim to reduce MACCE incidence.

The risk factors predicted in PG-HACKER score is able to give an empirical foundation and an understanding of the situation with an ability to deliver prompt prescriptions adhering to OMT. The resistance to insulin and glucose are the available targets for the attempt to reduce the incidence of MACCE following ACS in diabetic patients. The score is able to point out various conditions contributing independently to MACCE risk in the selected patients. The rigorous management of all the conditions by putting into practice robust treatment algorithms prove beneficial. The most important contributors to MACCE in diabetic patients post ACS is the increased possibility of HF (Marwick *et al.*, 2018).

The current research seems to indicate that diabetic patients are at an elevated risk for sudden cardiac death (SCD) even in the case that they have moderately reduced LVEF. The patient population included in the study benefits from detailed indications of ICD (Implantable cardioverter defibrillator) as compared to those dictated by the current guidelines. The study results

included the current estimates of SAD in patients suffering from ACS without systolic dysfunction (Chatterjee *et al.*, 2018).

The study conducted by Breuker et al recruit patients in the University Hospital, France from 2014 to 2017. The patients are suffering from type I and type II DM with the treatment of statin. The patients are reported to have an elevated CV risk matching the ESC guidelines for the year 2016. The LDL-cholesterol target was measured upon admission and it is considered to be the major risk factor for CVD because of its significant role to develop atherosclerosis. Statins as a treatment for lowering LDL cholesterol level is considerable and also to reduce CV events in patients with DM or non-DM patients (De Luca *et al.*, 2020). The study assesses the efficacy of cholesterol lowering therapy in patients with DM. For every 1.0mmol/L reduction in LDL-C obtained with statins, there is a significant decrease of 21% in major vascular events and 22% minimized risk of coronary events and 13% decrease in risk of vascular mortality.

The study, MONA LISA revealed that in the very high- risk subgroup only 4.2 % attained LDL-C target. Diabetes is associated with improved LDL-C control and the study further reveal LDL-C administration in patients at high risk of DM. The study reports that inclusion of woman without history of CAD, stroke or TIA was connected with lower attainment of LDL-C target but this gender difference is part of the other studies also despite the fact that no gender differences are observed in recommendations for lipid therapy. This gap in treatment or in fact reception of LDL-C target is multifactorial and the factors associated are *low dosage of prescription, lower level of continuity and discontinuous statin treatment in women* because of the low awareness in patients of CVD risks and high risk of intolerance.

Additionally, patients with no history of CAD or stroke had lower achievement of LDL-C target because of the fact that CV risk is not well presented and underestimated in such patients with less aggressive risk factor management. Study by Breuker et al is of the view that any patient with DM is at elevated risk of cardiovascular problems without any need for SCORE system as a risk estimation tool. The study of Budoff et al referd a second study by Haffner et al revealing that diabetic patients without MI had a risk of CHD as compared to those with MI without diabetes. There are relevant guidelines which acknowledge the risk heterogeneity with an inclusion of various treatment options and recommendations for patients with DM without other risk factors considering to be at lower risk. Guidelines also recommended that there is a need for further risk stratification in diabetic patients before the initiation of treatment. A pertinent question is asked in the study related to the screening of diabetic patients such as whether the patients with asymptomatic diabetes require routine screening for CHD? And if so how? Study by Budoff et al aims to review the evidence associated with non-invasive testing supported with the study by (Clerc *et al.*, 2018) for the stratification of asymptomatic patients with diabetes respective to CHD risk.

In patients with T2DM with normal LVEF, myocardial disease is inclusive of LV mass and diastolic function and decreased myocardial strain. Furthermore, T2DM patients are dispersed and heterogenous as related to age, gender, the duration of diabetes, and associated risk factors related to obesity or HTN. The interpretation of echocardiographic data in daily clinical practice becomes challenging in diabetic patients. There is an observed coexistence of HTN, T2DM and obesity and it made the task further difficult to isolate the existence of glucometabolic state to myocardial dysfunction. The research, therefore aims for cluster analysis for the identification of discriminated cardiac phenotypes in T2DM and to align these to clinical results.

Reported in the study by Galindo et al, the cardiac surgery patients and those who were critically ill develop hyperglycemia and were at increased risk for mortality. The patients of diabetes developing stress hyperglycemia during the surgery have negative outcomes compared to non-diabetic patients (Shah *et al.*, 2020). The mediators of stress such as stress hormones and cytokines and further the CNS interfere with secretion of insulin. There are negative outcomes related to hyperglycemia induced inflammation and oxidation stress and also prothrombic and vascular abnormalities.

There is an observed increase risk of cardiac and cerebrovascular incidence in patients with ACS and diabetes. To validate with success out of hospital outcomes remain problematic and no simple and effective tools exist for the patient population. The aim of the research is to assess factors utilizing a risk model for the incidence of heart diseases and heart failure in diabetic patients. Fine-Gray risk model was employed to ascertain the incidence of cardiac events leading to mortality. The risk factors as listed in the PG-HACKER score were utilized for the accurate prediction and of adverse cardiac events in ACS patients with diabetes.

The patients with diabetes are at elevated risk of cardiac events and LDL-C is considered as an established factor for cardiac failure. The patients of diabetes at high risk were given treatment of statins. Type I and type II diabetes patients receiving statins treatment are at high risk of cardiac failure as listed in 2016 ESC guidelines. The results of the study by Breuker et al reveal that risk of LDL-C targeted value was increased in women with history of coronary artery disease. Furthermore, the lipid lowering treatment must be increased in patients at high risk of diabetes and research specifies the gender differentiation because according to research women are at elevated risk of cardiovascular problems with the history of Diabetes Mellitus.

The American college of Cardiology evaluated the models mainly used for risk stratification in patients with DM and briefly discusses the data and recommendations in the research by Budoff et al. The document concisely lists the evidence with the use of non-invasive testing to select patients with DM. The new research highlights and acknowledge heterogeneity in risk with an inclusion of varied recommended treatments for diabetic patients. The study by Ernande et al seeks to associate cardiac phenotypes in DM patients with the patient profile and results using cluster analysis. Three distinct echocardiographic phenotypes of T2DM patients with diverse clinical profiles highlighting the value of left ventricular remodeling and dysfunction. Additionally, the study by Galindo et al is about the stress hyperglycemic patients who are not diabetic and to experience surgery increases risk and complications in patients and even death. Stress hormones and cytokines and CNS interfere with secretion of insulin and subsequent action.

## **Methodology**

The review of the available literature and published research journals is based on their relevancy, authenticity and credibility. The criteria opted for the inclusion of researches were that study should address the risk factors associated with diabetic patients admitted to cardiology. Further the research analyzed in detail striving for accurate judgments. The study should be published in the international authentic scientific journals and databases such as Elsevier, Springer, PubMed, Google Scholar, etc. Among the studies available those discussed in literature review are selected for the detailed analysis and relevant data.

## Findings

The findings obtained from the study of Baluja et al indicate that 783 (55.9%) patients with the MACCE event (417 of the selected resulted in death). Out of them, the number of patients with HF episodes during follow up were 374 (8 of them resulting in death) and 75 CVA episodes (no deaths reported). No significant differences observed respective to treatment except diuretic therapy. Lower LVEF data was associated with old patients with low BMI (body mass index).

The tables 2 given at page four of the research article indicate that Killip class and other factors reported in the study were associated with an increase in comorbidity. The models Predictive Fine-Gray models (CIF) showed that age and others discussed were associated with high MACCE incidence. The score indicated in PG-HACKER is an effective simple tool available and accessible. The conditions associated with negative outcomes must be identified for the future research seeking solution to counter the conditions were helpful in decreased MACCE incidence.

The patient population comprising of 756 patients admitted to the department were receiving statin treatment for less than 3 months. According to the 2016 guidelines, analyzed patients with DM and without any renal disease are listed at very high risk. The population profile is available in table 1 at page 197 who were admitted for the management of their diabetes. The patients without history of CAD, stroke or TIA found to be an increased risk of non-attainment of LDL-C target value.

The findings of the study by Budoff et al reveal that diabetic patients without MI had a 43% lower risk of developing CHD as compared to patients without diabetes with prior MI. The results of Budoff et al showed that diabetic patients were at decreased and lower risk of developing total CHD events.

The results further indicate that exercise stress testing as also reported in the study by (Poirier *et al.*, 2018) is able to identify diabetic patients with silent ischemia but whether it supports improved results in diabetic patients is not yet demonstrated. To conclude, authors are of the view that CTA screening results in modifications in 70% patients. The use of statin and lipid treatment results in reduction of CHD events.

As per the study of Ernande et al, the main analysis was performed on 745 of 842 patients and 88% of them completed echocardiographic information. There are similar variables observed between included and excluded patients except for the diabetes duration and BMI. The table 1 of research conducted by Ernande et al summarizes the characters of subgroups of T2DM alone associated with weight gain and HTN. The T2DM and HTN groups were older and had longer duration of diabetes. Table 2 of the research draws a comparison between echocardiographic data of four groups. LV morphology and systolic function remain unaltered by the presence of obesity and HTN. Contrary, groups with obesity and HTN had a considerable impact on diastolic function compared with the other groups. Galindo et al concludes that stress is an important risk factor that adversely effects the biological processes with almost reduced insulin action and this is due to the inactivity of pancreas to produce insulin resulting in hyperglycemia.

## **Discussion**

The first study uses a risk factor of PG-HACKER including age, gender and other factors and the study reports that the patients with diabetes and previous history of ACS are prone to have MACCE events when compared with any other outcome related to patient's mortality. The role of LVEF is important in the risk score of PG-HACKER and an important contributor to the research outcomes. The insulin resistance and glucose level are the targets to reduce the MACCE incidence following ACS in patients of diabetes. The second study by Breuker et al recruit patients of type I and type II DM treated with statin. The patients have an elevated risk cardiovascular risk matching the ESC guidelines for the 2016 year. The treatment with statin for lowering LDL cholesterol level is an important factor to reduce cardiovascular events in patients with DM. Further the study by Budoff et al is of the view that the relevant guidelines and recommendations for DM patients without other risk factors need relevant and further stratification in patients of diabetes before the initiation of treatment.

Additionally, in the study of Ernande et al T2DM is an individual risk factor for heart failure. The patients of diabetes are varied ranging from age, gender and associated risk factors and it becomes challenging to interpret echocardiographic data for T2DM patients and to assess the relative impact of the confounders on cardiac abnormalities. The study by Galindo et al reports cardiac surgery patients at increased risk for mortality are those with developed hyperglycemia. Further stress hormones and cytokines are there to interfere with the CNS with insulin secretion leading to glucose production and reduced intake of glucose in peripheral tissues.

## **Conclusion**

To conclude it is significant that patients of DM are at elevated risk of negative outcomes associated with CV disease. The risk factors taking in consideration the factor of age, gender, left ventricular function, peripheral atrial disease (Baluja et al, 2020) and others reported an increased death ratio in patients of diabetes with LDL-cholesterol as an established CV risk factor also. The study reports an increased risk of death in diabetic patients from HF (Breuker et al, 2018). The study of Budoff et al revealed that diabetic patients were at lower risk of CHD events while compared to patients with no diabetes but prior history of CHD.

As per the study of Ernande et al, T2DM is an individual risk factor for heart failure supported by the study of (Rahmani, Nakanishi and Budoff, 2016). Patients with T2DM present early cardiac modifications including diastolic dysfunction and reduced myocardial strain. While the percentage of patients who underwent cardiac surgery with a prior history of diabetes amounts to 30% to 40% (Galindo et al, 2018). Hyperglycemic patients as reported in the study are at increased risk of wound infections, kidney failure and lengthy hospital stay. The study further discusses the management of hyperglycemia and diabetes in patients admitted to cardiac surgery unit.

## References

- Baluja, A., Rodríguez-Mañero, M., Cordero, A., Kreidieh, B., Iglesias-Alvarez, D., García-Acuña, J. M., ... & López-Ratón, M. (2020). Prediction of major adverse cardiac, cerebrovascular events in patients with diabetes after acute coronary syndrome. *Diabetes and Vascular Disease Research*, 17(1), 1479164119892137.
- Breuker, C., Clement, F., Mura, T., Macioce, V., Castet-Nicolas, A., Audurier, Y., ... & Avignon, A. (2018). Non-achievement of LDL-cholesterol targets in patients with diabetes at very-high cardiovascular risk receiving statin treatment: incidence and risk factors. *International journal of cardiology*, 268, 195-199.
- Budoff, M. J., Raggi, P., Beller, G. A., Berman, D. S., Druz, R. S., Malik, S., ... & Imaging Council of the American College of Cardiology. (2016). Noninvasive cardiovascular risk assessment of the asymptomatic diabetic patient: the Imaging Council of the American College of Cardiology. *JACC: Cardiovascular Imaging*, 9(2), 176-192.
- Ernande, L., Audureau, E., Jellis, C. L., Bergerot, C., Henegar, C., Sawaki, D., ... & Ternacle, J. (2017). Clinical implications of echocardiographic phenotypes of patients with diabetes mellitus. *Journal of the American College of Cardiology*, 70(14), 1704-1716.
- Galindo, R. J., Fayfman, M., & Umpierrez, G. E. (2018). Perioperative management of hyperglycemia and diabetes in cardiac surgery patients. *Endocrinology and metabolism clinics of North America*, 47(1), 203.
- Savonitto, S., Morici, N., Nozza, A., Cosentino, F., Perrone Filardi, P., Murena, E., ... & Stähli, B. E. (2018). Predictors of mortality in hospital survivors with type 2 diabetes mellitus and acute coronary syndromes. *Diabetes and Vascular Disease Research*, 15(1), 14-23.
- Baeza-Román, A., de Miguel-Balsa, E., Latour-Pérez, J., & Carrillo-López, A. (2017). Predictive power of the grace score in population with diabetes. *International Journal of Cardiology*, 248, 73-76.
- Chatterjee, N. A., Moorthy, M. V., Pester, J., Schaecter, A., Panicker, G. K., Narula, D., ... & Albert, C. M. (2018). Sudden death in patients with coronary heart disease without severe systolic dysfunction. *JAMA cardiology*, 3(7), 591-600.
- Gulati, M., & Merz, C. N. B. (2016). Advances in lipid therapy: the role of lipid treatment in women in primary prevention. *Progress in cardiovascular diseases*, 59(2), 178-189.
- De Luca, L., Arca, M., Temporelli, P. L., Meessen, J., Riccio, C., Bonomo, P., ... & START Investigators. (2020). Current lipid lowering treatment and attainment of LDL targets recommended by ESC/EAS guidelines in very high-risk patients with established atherosclerotic cardiovascular disease: Insights from the START registry. *International Journal of Cardiology*.
- Rahmani, S., Nakanishi, R., & Budoff, M. J. (2016). Imaging atherosclerosis in diabetes: current state. *Current diabetes reports*, 16(11), 105.

Poirier, P., Bertrand, O. F., Leipsic, J., Mancini, G. J., Raggi, P., & Roussin, A. (2018). Screening for the presence of cardiovascular disease. *Canadian journal of diabetes*, 42, S170-S177.

Shah, N. J., Leis, A., Kheterpal, S., Englesbe, M. J., & Kumar, S. S. (2020). Association of intraoperative hyperglycemia and postoperative outcomes in patients undergoing non-cardiac surgery: a multicenter retrospective study. *BMC anesthesiology*, 20, 1-9.

Marwick, T. H., Ritchie, R., Shaw, J. E., & Kaye, D. (2018). Implications of underlying mechanisms for the recognition and management of diabetic cardiomyopathy. *Journal of the American College of Cardiology*, 71(3), 339-351.

Clerc, O. F., Fuchs, T. A., Stehli, J., Benz, D. C., Gräni, C., Messerli, M., ... & Kaufmann, P. A. (2018). Non-invasive screening for coronary artery disease in asymptomatic diabetic patients: a systematic review and meta-analysis of randomised controlled trials. *European Heart Journal-Cardiovascular Imaging*, 19(8), 838-846.