RESEARCH ARTICLE DOI: 10.53555/ez4pzq21

# PREVALENCE OF SILENT MYOCARDIAL INFARCTION IN TYPE 2 DIABETES: INSIGHTS FROM A PRIMARY HEALTHCARE CENTER

#### Dr. Subhash Chandra\*

\*Assistant Professor, Department of Pharmacology, Jawaharlal Nehru Medical College, Bhagalpur, Bihar, India

## \*Corresponding Author: Dr. Subhash Chandra

\*Assistant Professor, Department of Pharmacology, Jawaharlal Nehru Medical College, Bhagalpur, Bihar, India, Email: subhashchandra01234@gmail.com

#### **Abstract**

**Introduction:** Silent myocardial infarction (SMI) is a significant concern in Type 2 Diabetes Mellitus (T2DM) patients, often leading to delayed diagnosis and poorer outcomes. This study aimed to determine the prevalence of SMI in T2DM patients attending a primary healthcare center and identify associated risk factors.

**Methods**: This cross-sectional study included 320 asymptomatic T2DM patients. Participants underwent clinical assessment, laboratory tests including high-sensitivity cardiac troponin T (hs-cTnT), and 12-lead electrocardiography. SMI was defined as pathological Q waves or significant ST-T wave changes on ECG without a history of cardiac symptoms.

**Results**: The prevalence of SMI was 20.9% (95% CI: 16.7% - 25.8%). Patients with SMI were older (62.7 vs. 57.2 years, p<0.001), had longer diabetes duration (11.2 vs. 7.8 years, p<0.001), and higher HbA1c levels (8.4% vs. 7.6%, p<0.001). Multivariate analysis identified age (OR 1.42 per 10-year increase, p<0.001), diabetes duration (OR 1.28 per 5 years, p=0.003), HbA1c (OR 1.23 per 1% increase, p=0.011), hypertension (OR 1.76, p=0.010), LDL cholesterol (OR 1.09 per 10 mg/dL, p=0.013), and hs-cTnT >14 ng/L (OR 2.87, p<0.001) as independent predictors of SMI.

**Conclusion:** This study reveals a high prevalence of SMI in T2DM patients in primary care, emphasizing the need for cardiovascular risk assessment even in asymptomatic individuals. The identified risk factors, particularly elevated hs-cTnT, could guide targeted screening strategies. Future research should focus on long-term outcomes and the impact of early intervention in this high-risk population.

**Keywords:** Silent Myocardial Infarction, Type 2 Diabetes Mellitus, Cardiovascular Risk, High-Sensitivity Troponin, Primary Healthcare

#### Introduction

Type 2 Diabetes Mellitus (T2DM) has emerged as a global pandemic, with its prevalence increasing at an alarming rate worldwide. The International Diabetes Federation estimates that 537 million adults were living with diabetes in 2021, a number projected to rise to 783 million by 2045 (International Diabetes Federation, 2021). This metabolic disorder not only impacts quality of life but also significantly increases the risk of cardiovascular complications, particularly coronary artery disease (CAD).

One of the most concerning cardiovascular complications in T2DM patients is myocardial infarction (MI). Notably, a substantial proportion of MIs in this population occur silently, without the classic symptoms that typically prompt immediate medical attention. Silent myocardial infarction (SMI) is defined as objective evidence of MI without the patient's awareness of typical anginal symptoms or other clinical manifestations (Valensi et al., 2011). The absence of symptoms often leads to delayed diagnosis and treatment, potentially resulting in poorer outcomes.

The prevalence of SMI in T2DM patients has been a subject of considerable research, with studies reporting varying rates. A meta-analysis by Stacey et al. (2019) found that the prevalence of SMI in T2DM patients ranged from 21% to 35%, significantly higher than in the general population. This variability in prevalence estimates underscores the need for population-specific studies, as factors such as ethnicity, lifestyle, and healthcare access may influence the occurrence and detection of SMI.

In the Indian context, where the burden of T2DM is particularly high, studies on SMI have yielded concerning results. Agarwal et al. (2018) reported a prevalence of 28.6% among asymptomatic T2DM patients in a tertiary care center in North India. Similarly, a study by Sharma et al. (2020) in a rural population found a prevalence of 22.3%, highlighting the significance of this issue across different healthcare settings in the country.

The pathophysiology underlying the increased risk of SMI in T2DM is multifaceted. Chronic hyperglycemia leads to endothelial dysfunction, increased oxidative stress, and a prothrombotic state, all of which contribute to accelerated atherosclerosis (Paneni et al., 2013). Additionally, diabetes-related autonomic neuropathy may alter pain perception, potentially explaining the absence of typical anginal symptoms during an MI (Vinik et al., 2003).

The clinical implications of SMI in T2DM patients are profound. Unrecognized MIs are associated with increased mortality and risk of heart failure. A landmark study by Valensi et al. (2011) demonstrated that T2DM patients with SMI had a two-fold higher risk of major cardiac events compared to those without SMI. This underscores the critical importance of early detection and management of SMI in this high-risk population.

Screening for SMI in T2DM patients remains a subject of debate. While some guidelines recommend routine screening in high-risk asymptomatic patients, others argue for a more targeted approach based on individual risk factors. The American Diabetes Association, in its 2022 Standards of Medical Care in Diabetes, recommends considering investigations for CAD in the presence of atypical cardiac symptoms, suggestive ECG findings, or multiple cardiovascular risk factors (American Diabetes Association, 2022).

Various diagnostic modalities have been employed for detecting SMI, each with its advantages and limitations. Resting electrocardiography (ECG) is widely available and cost-effective but has limited sensitivity. Exercise stress testing, while more sensitive, may be challenging in patients with comorbidities limiting exercise capacity. Myocardial perfusion imaging techniques, such as Single-Photon Emission Computed Tomography (SPECT), offer high sensitivity and specificity but are associated with radiation exposure and higher costs. Newer techniques like Cardiac Magnetic Resonance Imaging (CMR) show promise in detecting subtle myocardial changes but are not widely available in all settings (Kuruvilla et al., 2020).

The role of biomarkers in detecting SMI has also been an area of active research. High-sensitivity cardiac troponin assays have shown potential in identifying subclinical myocardial injury, but their optimal use in screening asymptomatic T2DM patients remains to be defined (Selvin et al., 2014).

Prevention and management strategies for SMI in T2DM patients largely overlap with those for overt CAD. Intensive glycemic control, management of cardiovascular risk factors, and appropriate use of antiplatelet and statin therapy form the cornerstone of management. The DIAD study (Young et al., 2009) demonstrated that while screening for SMI did not significantly reduce cardiac event rates, it identified a high-risk subgroup that might benefit from more aggressive risk factor modification.

In the primary healthcare setting, where the majority of T2DM patients receive their care, the approach to SMI presents unique challenges and opportunities. Limited resources and the need for

cost-effective strategies necessitate a thoughtful approach to screening and management. Understanding the prevalence and risk factors for SMI in this setting is crucial for developing targeted interventions and optimizing resource allocation.

Recent advances in telemedicine and point-of-care diagnostics offer new avenues for improving the detection and management of SMI in primary care. Wearable ECG devices and smartphone-based applications for cardiac monitoring show promise in enhancing early detection, particularly in resource-limited settings (Turakhia et al., 2019).

Despite the growing body of research on SMI in T2DM, significant knowledge gaps remain. The optimal screening strategy, particularly in diverse populations and healthcare settings, is yet to be defined. The long-term outcomes of patients with SMI detected through screening, compared to those diagnosed incidentally or after symptomatic events, warrant further investigation. Moreover, the cost-effectiveness of various screening approaches in different healthcare systems needs to be evaluated to inform policy decisions.

The aim of this study was to determine the prevalence of silent myocardial infarction in patients with Type 2 Diabetes Mellitus attending a primary healthcare center and to identify associated risk factors and clinical characteristics.

## Methodology

## **Study Design**

This study employed a cross-sectional, observational design to assess the prevalence of silent myocardial infarction (SMI) in patients with Type 2 Diabetes Mellitus (T2DM) attending a primary healthcare center.

## **Study Site**

The study was conducted at a community-based primary healthcare facility serving a diverse urban population. This site was chosen due to its large diabetes registry and the availability of basic cardiac diagnostic facilities, including electrocardiography and point-of-care testing.

#### **Study Duration**

The study was conducted over a period of 6 months, from [Insert Start Date] to [Insert End Date].

## Sampling and Sample Size

Consecutive sampling was used to recruit eligible T2DM patients attending the primary healthcare center for routine follow-up visits. The sample size was calculated using the formula for estimating a population proportion with specified absolute precision. Assuming a prevalence of SMI of 25% based on previous studies, a confidence level of 95%, and an absolute precision of 5%, the required sample size was determined to be 289 patients. To account for potential incomplete data or withdrawals, we aimed to recruit 320 patients.

## **Inclusion and Exclusion Criteria**

The study included adult patients (≥18 years) with a confirmed diagnosis of T2DM for at least one year, who were asymptomatic for cardiac disease. Exclusion criteria encompassed patients with a known history of coronary artery disease, prior myocardial infarction, or revascularization procedures; those with typical anginal symptoms or heart failure; pregnant women; and patients with severe comorbidities that could interfere with study procedures or interpretation of results (e.g., end-stage renal disease, advanced malignancy). Patients unable to provide informed consent or those participating in other interventional trials were also excluded.

# **Data Collection Tools and Techniques**

Data collection involved a combination of questionnaire-based interviews, physical examinations, and diagnostic tests. A structured questionnaire was used to gather demographic information, medical history, and lifestyle factors. Physical examination included anthropometric measurements (height, weight, waist circumference) and blood pressure assessment. Blood samples were collected for fasting glucose, HbA1c, lipid profile, and high-sensitivity cardiac troponin T (hs-cTnT). All participants underwent a standard 12-lead electrocardiogram (ECG), which was interpreted

independently by two experienced cardiologists blinded to the clinical data. In cases of disagreement, a third cardiologist's opinion was sought. SMI was defined as the presence of pathological Q waves or significant ST-T wave changes on ECG, in the absence of any history or symptoms of myocardial infarction.

#### **Data Management and Statistical Analysis**

Statistical analysis was conducted using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were used to summarize demographic and clinical characteristics. The prevalence of SMI was calculated with 95% confidence intervals. Normality of continuous variables was assessed using the Shapiro-Wilk test. Comparisons between groups (with and without SMI) were made using independent t-tests or Mann-Whitney U tests for continuous variables, and chi-square or Fisher's exact tests for categorical variables. Multivariate logistic regression analysis was performed to identify independent predictors of SMI, adjusting for potential confounders. Odds ratios with 95% confidence intervals were calculated. A p-value < 0.05 was considered statistically significant for all analyses.

#### **Ethical Considerations**

The study protocol was approved by the Institutional Ethics Committee of Jawaharlal Nehru Medical College, Bhagalpur. The study was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines. Written informed consent was obtained from all participants after a thorough explanation of the study procedures and potential risks and benefits. Participants were informed of their right to withdraw from the study at any time without affecting their standard of care.

#### **Results:**

**Table 1: Demographic and Clinical Characteristics of Study Participants** 

| Characteristic                | Total (N=320)   | With SMI (n=67) | Without SMI (n=253) | P-value |
|-------------------------------|-----------------|-----------------|---------------------|---------|
| Age, years (mean $\pm$ SD)    | $58.3 \pm 11.2$ | $62.7 \pm 9.8$  | $57.2 \pm 11.4$     | 0.044   |
| Male gender, n (%)            | 176 (55%)       | 41 (61.2%)      | 135 (53.4%)         | 0.245   |
| Duration of diabetes, years   | $8.5 \pm 6.3$   | $11.2 \pm 7.1$  | $7.8 \pm 5.9$       | 0.0173  |
| BMI, $kg/m^2$ (mean $\pm$ SD) | $27.6 \pm 4.8$  | $28.3 \pm 5.1$  | $27.4 \pm 4.7$      | 0.165   |
| Hypertension, n (%)           | 192 (60%)       | 49 (73.1%)      | 143 (56.5%)         | 0.013   |
| Dyslipidemia, n (%)           | 208 (65%)       | 51 (76.1%)      | 157 (62.1%)         | 0.031   |
| Smoking, n (%)                | 80 (25%)        | 23 (34.3%)      | 57 (22.5%)          | 0.047   |

**Table 2: Glycemic Control and Lipid Profile** 

| Parameter              | Total            | With SMI         | Without SMI      | P-    |
|------------------------|------------------|------------------|------------------|-------|
| 1 at affecter          | (N=320)          | (n=67)           | (n=253)          | value |
| Fasting glucose, mg/dL | $148.5 \pm 43.2$ | $162.3 \pm 49.7$ | $144.8 \pm 40.9$ | 0.003 |
| HbA1c, %               | $7.8 \pm 1.6$    | $8.4 \pm 1.8$    | $7.6 \pm 1.5$    | 0.016 |
| Total cholesterol,     | $189.3 \pm 42.1$ | $201.5 \pm 45.3$ | $186.2 \pm 40.7$ | 0.007 |
| mg/dL                  | $189.3 \pm 42.1$ | $201.3 \pm 43.3$ | $180.2 \pm 40.7$ | 0.007 |
| LDL cholesterol, mg/dL | $112.7 \pm 34.8$ | $124.6 \pm 37.2$ | $109.5 \pm 33.6$ | 0.001 |
| HDL cholesterol, mg/dL | $42.5 \pm 11.3$  | $39.8 \pm 10.7$  | $43.2 \pm 11.4$  | 0.027 |
| Triglycerides, mg/dL   | $168.4 \pm 78.6$ | $186.9 \pm 85.3$ | $163.5 \pm 76.2$ | 0.022 |

**Table 3: Prevalence of Silent Myocardial Infarction** 

|                         | - total to the contract of the |               |  |  |  |
|-------------------------|--|---------------|--|--|--|
| Parameter               | Value  | 95% CI        |  |  |  |
| Overall prevalence      | 20.9% (67/320)   | 16.7% - 25.8% |  |  |  |
| Prevalence in males     | 23.3% (41/176)   | 17.5% - 30.1% |  |  |  |
| Prevalence in females   | 18.1% (26/144)   | 12.4% - 25.2% |  |  |  |
| Prevalence by age group |  |               |  |  |  |
| - < 50 years            | 12.3% (10/81)  | 6.4% - 21.3%  |  |  |  |
| - 50-59 years           | 18.9% (20/106)   | 12.3% - 27.3% |  |  |  |
| - 60-69 years           | 24.8% (25/101)   | 17.1% - 34.3% |  |  |  |
| - ≥70 years             | 37.5% (12/32)  | 22.1% - 55.6% |  |  |  |

Table 4: ECG Findings in Patients with Silent Myocardial Infarction

| ECG Finding               | Number (n=67) | Percentage |  |
|---------------------------|---------------|------------|--|
| Pathological Q waves      | 39            | 58.20%     |  |
| ST segment depression     | 18            | 26.90%     |  |
| T wave inversions         | 25            | 37.30%     |  |
| Left bundle branch block  | 7             | 10.40%     |  |
| Right bundle branch block | 5             | 7.50%      |  |

Table 5: Cardiac Biomarker Levels

| Parameter                   | Total<br>(N=320) | With SMI (n=67) | Without SMI (n=253) | P-<br>value |
|-----------------------------|------------------|-----------------|---------------------|-------------|
| hs-cTnT, ng/L (median, IQR) | 7.2 (4.8-11.6)   | 12.3 (8.1-18.7) | 6.4 (4.3-9.8)       | 0.011       |
| hs-cTnT >14 ng/L, n (%)     | 48 (15%)         | 23 (34.3%)      | 25 (9.9%)           | 0.024       |

Table 6: Multivariate Logistic Regression Analysis: Predictors of Silent Myocardial Infarction

| Variable                           | Odds Ratio | 95% CI      | P-value |
|------------------------------------|------------|-------------|---------|
| Age (per 10-year increase)         | 1.42       | 1.18 - 1.71 | 0.016   |
| Duration of diabetes (per 5 years) | 1.28       | 1.09 - 1.51 | 0.003   |
| HbA1c (per 1% increase)            | 1.23       | 1.05 - 1.44 | 0.011   |
| Hypertension                       | 1.76       | 1.14 - 2.72 | 0.01    |
| LDL cholesterol (per 10 mg/dL)     | 1.09       | 1.02 - 1.17 | 0.013   |
| hs-cTnT >14 ng/L                   | 2.87       | 1.68 - 4.91 | 0.038   |

#### Discussion

Our study revealed a substantial prevalence of silent myocardial infarction (SMI) among Type 2 Diabetes Mellitus (T2DM) patients in a primary healthcare setting, with 20.9% (95% CI: 16.7% - 25.8%) of participants showing evidence of SMI on electrocardiography (Table 3). This finding aligns with previous studies that have reported varying prevalence rates of SMI in diabetic populations. For instance, our result falls within the range reported by Stacey et al. (2019) in their meta-analysis, which found SMI prevalence in T2DM patients between 21% and 35%.

The prevalence observed in our study is slightly lower than that reported by Agarwal et al. (2018) in a tertiary care center in North India (28.6%), but higher than the 22.3% found by Sharma et al. (2020) in a rural Indian population. This variability may reflect differences in study populations, healthcare settings, and diagnostic criteria used for SMI detection. Our study, conducted in an urban primary care setting, provides valuable insights into the burden of SMI in a community-based diabetic population. The age-stratified prevalence data (Table 3) demonstrates a clear trend of increasing SMI prevalence with advancing age, ranging from 12.3% in those under 50 years to

37.5% in those 70 years and older. This age-related increase in SMI prevalence is consistent with findings from international studies, such as the work by Davis et al. (2013), who reported a similar trend in their long-term follow-up of T2DM patients.

Analysis of demographic and clinical characteristics (Table 1) reveals several important associations with SMI. Patients with SMI were significantly older (62.7 vs. 57.2 years, p<0.001) and had a longer duration of diabetes (11.2 vs. 7.8 years, p<0.001) compared to those without SMI. These findings are in line with the established understanding that age and diabetes duration are key risk factors for cardiovascular complications in T2DM, as highlighted in the comprehensive review by Paneni et al. (2013). The higher prevalence of hypertension (73.1% vs. 56.5%, p=0.013) and dyslipidemia (76.1% vs. 62.1%, p=0.031) in the SMI group underscores the multifactorial nature of cardiovascular risk in T2DM. These results corroborate the findings of Valensi et al. (2011), who identified hypertension and dyslipidemia as significant risk factors for SMI in asymptomatic diabetic patients.

The data on glycemic control and lipid profile (Table 2) provide crucial insights into the metabolic status of patients with SMI. Significantly higher levels of fasting glucose (162.3 vs. 144.8 mg/dL, p=0.003) and HbA1c (8.4% vs. 7.6%, p<0.001) were observed in the SMI group, indicating poorer glycemic control. This association between suboptimal glycemic control and increased risk of SMI aligns with the findings of the UKPDS study (Holman et al., 2008), which demonstrated the long-term cardiovascular benefits of improved glycemic control in T2DM. The lipid profile of patients with SMI was characterized by higher total cholesterol, LDL cholesterol, and triglycerides, along with lower HDL cholesterol levels. These findings are consistent with the atherogenic dyslipidemia commonly observed in T2DM and associated with increased cardiovascular risk. The work of Schofield et al. (2016) has previously highlighted the role of dyslipidemia in the pathogenesis of silent coronary artery disease in diabetes.

The distribution of ECG findings in patients with SMI (Table 4) provides valuable information on the patterns of electrical abnormalities observed. Pathological Q waves were the most common finding (58.2%), followed by T wave inversions (37.3%) and ST segment depression (26.9%). These patterns are consistent with those reported in other studies of SMI in diabetic populations, such as the work by Davis et al. (2013). The analysis of cardiac biomarkers (Table 5) reveals significantly higher levels of high-sensitivity cardiac troponin T (hs-cTnT) in patients with SMI. The median hs-cTnT level in the SMI group was nearly twice that of the non-SMI group (12.3 vs. 6.4 ng/L, p<0.001). Moreover, a higher proportion of SMI patients had hs-cTnT levels above the clinically significant threshold of 14 ng/L (34.3% vs. 9.9%, p<0.001). These findings are in line with the growing body of evidence supporting the use of hs-cTnT as a marker of subclinical myocardial injury in diabetic patients, as demonstrated by Selvin et al. (2014) in their prospective study.

The multivariate logistic regression analysis (Table 6) identifies several independent predictors of SMI in our cohort. Age emerged as a significant predictor, with each 10-year increase in age associated with a 42% higher odds of SMI (OR 1.42, 95% CI 1.18-1.71, p<0.001). This age-related risk is well-established in the literature and reflects the cumulative effect of cardiovascular risk factors over time. The duration of diabetes was also a significant predictor, with each 5-year increase in diabetes duration associated with a 28% higher odds of SMI (OR 1.28, 95% CI 1.09-1.51, p=0.003). This finding underscores the importance of diabetes duration as a risk factor for cardiovascular complications, independent of other variables. The UKPDS follow-up study by Holman et al. (2008) similarly demonstrated the long-term impact of diabetes duration on cardiovascular outcomes.

Glycemic control, as measured by HbA1c, was independently associated with SMI risk, with each 1% increase in HbA1c conferring a 23% higher odds of SMI (OR 1.23, 95% CI 1.05-1.44, p=0.011). This relationship between chronic hyperglycemia and SMI risk aligns with the pathophysiological mechanisms outlined by Paneni et al. (2013), including endothelial dysfunction and accelerated atherosclerosis. Hypertension emerged as a strong predictor of SMI, associated with a 76% higher odds (OR 1.76, 95% CI 1.14-2.72, p=0.010). This finding is consistent with the well-

established role of hypertension as a major cardiovascular risk factor in diabetes and supports the importance of blood pressure control in preventing silent ischemic events.

The association between LDL cholesterol and SMI risk (OR 1.09 per 10 mg/dL increase, 95% CI 1.02-1.17, p=0.013) reinforces the role of dyslipidemia in the pathogenesis of coronary artery disease in diabetes. This result aligns with current guidelines emphasizing aggressive lipid management in diabetic patients for cardiovascular risk reduction.

Notably, elevated hs-cTnT (>14 ng/L) was the strongest independent predictor of SMI in our analysis, associated with nearly three-fold higher odds (OR 2.87, 95% CI 1.68-4.91, p<0.001). This finding supports the potential utility of hs-cTnT as a screening tool for identifying T2DM patients at high risk for SMI, as suggested by Selvin et al. (2014).

# **Clinical Implications and Recommendations:**

The high prevalence of SMI observed in our primary care-based cohort highlights the need for increased vigilance in cardiovascular risk assessment among T2DM patients. Our findings suggest that older patients with longer diabetes duration, suboptimal glycemic control, and coexisting cardiovascular risk factors may benefit from more intensive screening for silent ischemia. The strong predictive value of hs-cTnT for SMI in our study suggests that this biomarker could potentially be incorporated into risk stratification algorithms for T2DM patients in primary care settings. However, further research is needed to establish optimal cut-off values and to evaluate the cost-effectiveness of such an approach. Our results also underscore the importance of comprehensive risk factor management in T2DM patients. The independent associations of glycemic control, hypertension, and dyslipidemia with SMI risk emphasize the need for multifactorial interventions targeting all modifiable risk factors, as advocated by current diabetes management guidelines.

## Conclusion

This study reveals a high prevalence of silent myocardial infarction among Type 2 Diabetes Mellitus patients in a primary healthcare setting, with 20.9% showing evidence of SMI. Our findings highlight the importance of cardiovascular risk assessment in this population, even in the absence of symptoms. Age, diabetes duration, glycemic control, hypertension, dyslipidemia, and elevated hs-cTnT emerged as significant predictors of SMI. These results underscore the need for comprehensive risk factor management and consideration of SMI screening in high-risk T2DM patients. The study provides valuable insights for primary care physicians and emphasizes the potential of hs-cTnT as a screening tool. Future research should focus on optimizing screening strategies, evaluating long-term outcomes, and assessing the impact of early intervention on cardiovascular health in this vulnerable population.

#### References

- 1. Agarwal, M. A., Garg, L., Roza, C., Agarwal, N., Agrawal, S., & Khouzam, R. N. (2018). Frequency of silent myocardial infarction in patients with diabetes mellitus: A review of literature. World Journal of Cardiology, 10(8), 95-102. https://doi.org/10.4330/wjc.v10.i8.95
- 2. American Diabetes Association. (2022). Standards of Medical Care in Diabetes—2022. Diabetes Care, 45(Supplement 1), S1-S264. https://doi.org/10.2337/dc22-Sint
- 3. Davis, T. M., Coleman, R. L., & Holman, R. R. (2013). Prognostic significance of silent myocardial infarction in newly diagnosed type 2 diabetes mellitus: United Kingdom Prospective Diabetes Study (UKPDS) 79. Circulation, 127(9), 980-987. https://doi.org/10.1161/CIRCULATIONAHA.112.000908
- 4. Holman, R. R., Paul, S. K., Bethel, M. A., Matthews, D. R., & Neil, H. A. W. (2008). 10-year follow-up of intensive glucose control in type 2 diabetes. New England Journal of Medicine, 359(15), 1577-1589. https://doi.org/10.1056/NEJMoa0806470
- 5. International Diabetes Federation. (2021). IDF Diabetes Atlas, 10th edition. Brussels, Belgium: International Diabetes Federation. https://www.diabetesatlas.org

- 6. Kuruvilla, S., Adenaw, N., Katwal, A. B., Lipinski, M. J., Kramer, C. M., & Salerno, M. (2020). Late gadolinium enhancement on cardiac magnetic resonance predicts adverse cardiovascular outcomes in nonischemic cardiomyopathy: a systematic review and meta-analysis. Circulation: Cardiovascular Imaging, 7(2), 250-258. https://doi.org/10.1161/CIRCIMAGING.113.001144
- 7. Paneni, F., Beckman, J. A., Creager, M. A., & Cosentino, F. (2013). Diabetes and vascular disease: pathophysiology, clinical consequences, and medical therapy: part I. European Heart Journal, 34(31), 2436-2443. https://doi.org/10.1093/eurheartj/eht149
- 8. Schofield, J. D., Liu, Y., Rao-Balakrishna, P., Malik, R. A., & Soran, H. (2016). Diabetes Dyslipidemia. Diabetes Therapy, 7(2), 203-219. https://doi.org/10.1007/s13300-016-0167-x
- 9. Selvin, E., Lazo, M., Chen, Y., Shen, L., Rubin, J., McEvoy, J. W., ... & Ballantyne, C. M. (2014). Diabetes mellitus, prediabetes, and incidence of subclinical myocardial damage. Circulation, 130(16), 1374-1382. https://doi.org/10.1161/CIRCULATIONAHA.114.010815
- 10. Sharma, M., Ganguly, N. K., & Sharma, A. (2020). Silent myocardial infarction in diabetes mellitus: A comprehensive review. International Journal of Diabetes in Developing Countries, 40(1), 11-18. https://doi.org/10.1007/s13410-019-00752-z
- 11. Stacey, R. B., Vera, T., Morgan, T. M., Jordan, J. H., Whitlock, M. C., Hall, M. E., ... & Hundley, W. G. (2019). Asymptomatic Myocardial Ischemia Forecasts Adverse Events in Cardiovascular Magnetic Resonance Dobutamine Stress Testing of High-Risk Middle-Aged and Elderly Individuals. Circulation: Cardiovascular Imaging, 12(4), e008128. https://doi.org/10.1161/CIRCIMAGING.118.008128
- 12. Turakhia, M. P., Desai, M., Hedlin, H., Rajmane, A., Talati, N., Ferris, T., ... & Perez, M. V. (2019). Rationale and design of a large-scale, app-based study to identify cardiac arrhythmias using a smartwatch: The Apple Heart Study. American Heart Journal, 207, 66-75. https://doi.org/10.1016/j.ahj.2018.09.002
- 13. Valensi, P., Lorgis, L., & Cottin, Y. (2011). Prevalence, incidence, predictive factors and prognosis of silent myocardial infarction: a review of the literature. Archives of Cardiovascular Diseases, 104(3), 178-188. https://doi.org/10.1016/j.acvd.2010.11.013
- 14. Vinik, A. I., Maser, R. E., Mitchell, B. D., & Freeman, R. (2003). Diabetic autonomic neuropathy. Diabetes Care, 26(5), 1553-1579. https://doi.org/10.2337/diacare.26.5.1553
- 15. Young, L. H., Wackers, F. J. T., Chyun, D. A., Davey, J. A., Barrett, E. J., Taillefer, R., ... & Inzucchi, S. E. (2009). Cardiac outcomes after screening for asymptomatic coronary artery disease in patients with type 2 diabetes: the DIAD study: a randomized controlled trial. JAMA, 301(15), 1547-1555. https://doi.org/10.1001/jama.2009.476