Real-World Cardiovascular Event Rates Among High-Risk Adults with Type 2 Diabetes Mellitus

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Abstract

This investigation ascertained the incidence and time to first non-fatal myocardial infarction (MI) or stroke among adults with type 2 diabetes mellitus (T2DM) at high risk for cardiovascular disease (CVD) over 3 and 5 years.

A retrospective cohort study used data from the US population-based Study to Help Improve Early evaluation and management of risk factors Leading to Diabetes (SHIELD). High-risk respondents with T2DM were stratified into 2 cohorts: 1) established CVD with age ≥40 years, prior MI, prior stroke, atherosclerosis, or peripheral vascular disease, and 2) multiple risk factors (men ≥55 years and women ≥60 years and ≥1 risk factors of hyperlipidemia, hypertension, or current smoking, without prior history of CVD). Proportion of respondents self-reporting a new MI or stroke was calculated, and multivariate discrete logistic hazards models for 3 and 5 years of follow-up were developed.

Among 2122 T2DM respondents, 56.5% had established CVD (mean age = 65 years, 45% men); 43.5% had no established CVD but multiple risk factors (mean age = 68 years, 49% men). The established CVD cohort had a new MI or stroke event rate of 16.7% during a 3-year follow up period and 20.5% during the 5-year follow-up. For the multiple risk factors cohort, 17.6% within 3 years and 24.5% within 5 years had an incident MI or stroke. Hazard ratio (HR) of incident MI was 2.1 times higher (95% CI: 1.6–2.8) within 3 years and 1.9 times higher (1.5–2.4) within 5 years of follow-up, after adjusting for gender, age, obesity, duration of diabetes, and comorbidities, among the established CVD cohort than among the multiple risk factors cohort (p <0.001). HR of incident stroke was 2.2 (1.4–3.5) and 1.8 (1.2–2.7) times higher within 3 and 5 years, respectively, after adjustment among the established CVD cohort than among the multiple risk factors cohort (p <0.01). In this large US population-based study, individuals with T2DM at risk for CVD had a significant incidence of MI and stroke. Respondents with T2DM with established CVD are at higher risk than those with no CVD but with multiple risk factors.

Background

- Cardiovascular disease (CVD) is a major complication of type 2 diabetes mellitus (T2DM), and mortality from CVD is increased 2–3 fold in persons with T2DM compared with the general population[1]
- The risk of CVD and stroke is 2 to 4 times higher among people with diabetes than among people without diabetes[2]
- National Cholesterol Education Program Adult Treatment Panel III guidelines classified diabetes mellitus as a coronary heart disease (CHD) risk equivalent, and individuals with diabetes or diagnosis of CHD are at high risk of CV event[3]
- It is important to determine whether incidence of CVD events has changed in recent years and whether incidence varies based on history of CVD and risk factors among adults with T2DM

Objective

- To ascertain the incidence and time to first non-fatal myocardial infarction (MI) or stroke over 3 and 5 years among adults with T2DM at high risk for CVD using the large US population-based **S**tudy to **H**elp Improve **E**arly evaluation and management of risk factors **L**eading to **D**iabetes (SHIELD) study

Methods

Study Design

- Retrospective cohort study among SHIELD respondents with T2DM and at risk of CVD events
- SHIELD is a 5-year population-based survey conducted to better understand the risk for the development of diabetes, as well as diabetes disease burden
  - Based upon a screening questionnaire mailed to 200,000 nationally representative households (TNS NFO Household Panel), responses for 211,097 adults from 127,420 households were obtained (64% response rate)
  - A baseline survey was sent to 22,001 selected individuals derived from the screening respondents. Since 2005, annual SHIELD surveys have captured self-reported information on health status, attitudes and behaviors, quality of life, and comorbid conditions from this representative sample of the US population
  - The response rate for the baseline survey was 72%, and response rates to the 2005–2009 annual follow-up surveys ranged from 69% to 75%. Methodology and research findings from SHIELD have been published previously[4]

Study Population

- For this analysis, respondents were 40 years of age or older at baseline
- Self-reported diagnosis of T2DM was based on being "told by a doctor, nurse or other healthcare professional that you have type 2 diabetes"
- Respondents had to complete the baseline survey and at least 1 of the follow-up surveys

Study Population (Continued)

- Saxagliptin Assessment of Vascular Outcomes Recorded in patients with diabetes mellitus (SAVOR) is an ongoing, multicenter, double-blind, placebo controlled, Phase IV outcomes trial to evaluate the effect of saxagliptin on the incidence of cardiovascular death, MI, or ischemic stroke in patients with T2DM. Similar inclusion criteria from SAVOR were applied to identify respondents at high risk of CV events and stratified into 2 cohorts:
  - Established CVD cohort was T2DM respondents with at least 1 of the following self-reported conditions at baseline:
    - Heart disease/heart attack
    - Narrow or blocked arteries
    - Circulation problems of any kind
    - Stroke
  - Multiple risk factors cohort was T2DM respondents without established CVD but with the following risk factors at baseline:
    - Men ≥55 years and women ≥60 years of age
    - At least 1 additional risk factor of:
      - Cholesterol problems
      - High blood pressure/hypertension
      - Current smoker

Study Measures

- CVD events were reported at baseline as "ever been told by a doctor, nurse or other healthcare professional that you had a heart attack or stroke". Only non-fatal MI and stroke events were captured
- In the subsequent 5 years, any new reported MI or stroke was captured. For respondents with a history of MI at baseline, only stroke events were counted as incident events during follow-up and vice versa

Statistical Analyses

- Number of new MIs or strokes reported over 3 years and 5 years was tabulated for each cohort
- Discrete logistic hazard survival models for 3 and 5 years were constructed to estimate conditional odds of CVD event, adjusting for age, gender, obesity, duration of T2DM, arthritis, asthma, chronic obstructive pulmonary disease (COPD), and kidney problems
- Survival models were constructed for time to first MI and time to first stroke independently, as the CVD event outcome was conditional based on prior history of the CVD event
- Comparisons between cohorts at baseline were conducted using chi-square tests for categorical variables and *t*-tests for continuous variables

Results

- In total, 2122 respondents with T2DM were included in the study; 1198 (56.5%) respondents had established CVD, and 924 (43.5%) had no established CVD but multiple risk factors

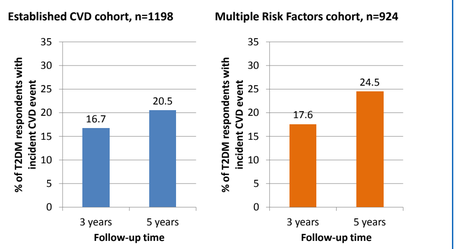
Table 1. Baseline characteristics of respondents with T2DM with and without established CVD

Characteristic	Established CVD cohort (n = 1198)	Multiple risk factors cohort (n = 924)
Age, years, mean (SD)	64.6 (11.4)	68.0 (7.7)
Men, %	45.2	48.9
Body mass index, kg/m², %		
Normal weight, ≤25.0 kg/m²	11.8	12.5
Overweight, 25.0–29.9 kg/m²	26.2	33.4
Obese, ≥30 kg/m²	62.0	54.1
Comorbid conditions at baseline, %		
Heart disease/heart attack	55.8	0
Stroke	16.5	0
Heart bypass surgery	14.5	1.8
Angioplasty	25.4	2.6
Cholesterol problems	81.6	79.0
Hypertension	75.8	79.0
Currently smoke, %	19.1	14.2

- Mean age was approximately 65–68 years, and the majority of respondents were obese at baseline for both cohorts (Table 1)

CVD Event Incidence

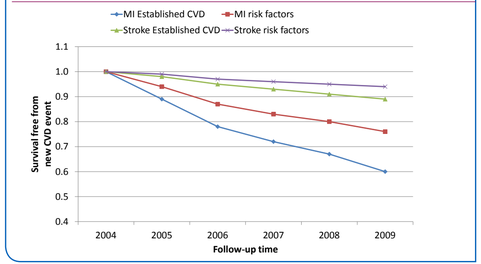
Figure 1. Proportion of respondents with T2DM with new non-fatal MI or stroke within 3 and 5 years of follow-up, stratified by CVD risk cohort



- Among the established CVD cohort, 200 (16.7%) respondents experienced a new CVD event within 3 years, and 245 (20.5%) respondents experienced a new CVD event within 5 years (Figure 1)
- Among the multiple risk factors cohort, 163 (17.6%) respondents experienced a new CVD event within 3 years, and 226 (24.5%) respondents experienced a new CVD event within 5 years (Figure 1)

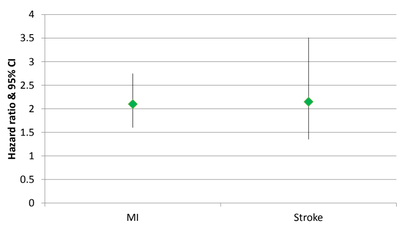
Time to First CVD Event

Figure 2. Kaplan-Meier curves for time to first new, non-fatal MI or stroke among respondents with T2DM at risk for CVD events



- Time to first non-fatal MI was steep for both cohorts, with 60% of the established CVD cohort and 76% of the multiple risk factors cohort free of MI at 5 years (Figure 2)
- Non-fatal stroke had slower time trajectory in both cohorts, with 89%–94% of the cohorts free of these CVD events at 5 years

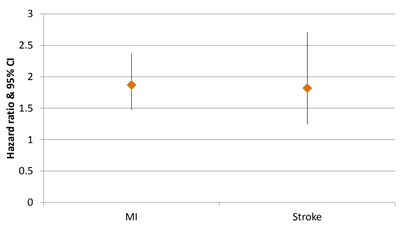
Figure 3. Adjusted discrete logistic hazard ratios* for likelihood of new non-fatal MI or stroke within 3 years between the established CVD cohort and multiple risk factors cohort



*Adjusted for age, gender, obesity, duration of T2DM, arthritis, asthma, COPD, and kidney problems

- Likelihood of MI or stroke was double within 3 years for the established CVD cohort compared with the multiple risk factors cohort, after adjusting for patient characteristics and comorbid conditions (Figure 3)
- Hazard rate (risk of CVD events) through 3 years peaked at:
  - For established CVD cohort, 0.38 for MI and 0.09 for stroke
  - For multiple risk factors cohort, 0.18 for MI and 0.04 for stroke

Figure 4. Adjusted discrete logistic hazard ratios* for likelihood of new non-fatal MI or stroke within 5 years between the established CVD cohort and multiple risk factors cohort



*Adjusted for age, gender, obesity, duration of T2DM, arthritis, asthma, COPD, and kidney problems

- Over 5 years, the likelihood of MI or stroke was 1.8–1.9 times higher in the established CVD cohort than in the multiple risk factors cohort, after adjusting for patient characteristics and comorbid conditions (Figure 4)
- Hazard rate (incidence) through 5 years peaked at:
  - For established CVD cohort, 0.50 for MI and 0.11 for stroke
  - For multiple risk factors cohort, 0.28 for MI and 0.06 for stroke

Limitations

- Diagnosis of diabetes, CVD events, and other comorbid conditions were self-reported and could not be validated with medical record review or administrative claims data
- For respondents with a baseline history of CVD events (eg, MI), only CVD events of a different type (eg, stroke) than the original event could be counted as incident events over the follow-up period. This may underestimate the number of incident events in the established CVD cohort and explain why the incidence is slightly lower in the established CVD cohort than in the multiple risk factor cohort
- Fatal MI and stroke were not captured in the SHIELD study and hence not included in the analysis
- Household panels, like the SHIELD study, tend to under-represent the very wealthy and very poor segments of the population and do not include military or institutionalized individuals

Summary

- Using the latest data from a large US study, adults with T2DM and at risk for CVD had significant incidence of MI and stroke
- Approximately 17% of respondents with T2DM and established CVD had an incident MI or stroke within 3 years and 21% within 5 years. Approximately 18% of respondents with T2DM and no established CVD but with multiple risk factors had an incident MI or stroke within 3 years and 25% within 5 years
- Time to first CVD event was steepest for MI in both cohorts. Stroke in both cohorts had a lower incidence of about 6%–11% within 3 and 5 years

Conclusions

- Self-reported incident non-fatal CVD events (MI or stroke) occurred at a high rate over 3 and 5 years among adults with T2DM and established CVD or with multiple risk factors, emphasizing the existence of very-high-risk subgroups among adults with T2DM
- Dipeptidyl peptidase-4 (DPP-4) inhibitors, such as saxagliptin, are currently being assessed for potential CV benefit in large outcomes trials, like SAVOR

References

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2. Centers for Disease Control Prevention. National diabetes fact sheet, 2011
3. Grundy SM, et al. *Circulation* 2004;110:227–239
4. Bays HE, et al. *BMC Public Health* 2007;7:277

List of Abbreviations

CHD	Coronary heart disease
COPD	Chronic obstructive pulmonary disease
CVD	Cardiovascular disease
DPP-4	Dipeptidyl peptidase-4
MI	Myocardial infarction
SAVOR	Saxagliptin Assessment of Vascular Outcomes Recorded in patients with diabetes mellitus
SHIELD	Study to Help Improve Early evaluation and management of risk factors Leading to Diabetes
T2DM	Type 2 diabetes mellitus
TNS NFO	Taylor Nelson Sofres National Family Opinion
US	United States

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