Cardiovascular Diabetology

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High proportion of undiagnosed diabetes in patients surgically treated for infrarenal abdominal aortic aneurysm: findings from the multicentre Norwegian Aortic Aneurysm and Diabetes (ABANDIA) Study

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Abstract

Background The aim was to investigate the total prevalence of known and undiagnosed diabetes mellitus (DM), and the association of DM with perioperative complications following elective, infrarenal, open surgical (OSR) or endovascular (EVAR), Abdominal Aortic Aneurysm (AAA) repair.

Methods In this Norwegian prospective multicentre study, 877 patients underwent preoperative screening for DM by HbA_{1c} measurements from November 2017 to December 2020. Diabetes was defined as screening detected $HbA_{1c} \geq 48$ mmol/mol (6.5%) or previously diagnosed diabetes. The association of DM with in-hospital complications, length of stay, and 30-day mortality rate were evaluated using adjusted and unadjusted logistic regression models.

Results The total prevalence of DM was 15% (95% CI 13%,17%), of which 25% of the DM cases (95% CI 18%,33%) were undiagnosed upon admission for AAA surgery. The OSR to EVAR ratio was 52% versus 48%, with similar distribution among DM patients, and no differences in the prevalence of known and undiagnosed DM in the EVAR versus the OSR group. Total 30-day mortality rate was 0.6% (5/877). Sixty-six organ-related complications occurred in 58 (7%) of the patients. DM was not statistically significantly associated with a higher risk of in-hospital organ-related complications (OR 1.23, 95% CI 0.57,2.39, $p=0.57$), procedure-related complications (OR 1.48, 95% CI 0.79,2.63, $p=0.20$), 30-day mortality ($p=0.09$) or length of stay (HR 1.06, 95% CI 0.88,1.28, $p=0.54$). According to post-hoc-analyses, organ-related complications were more frequent in patients with newly diagnosed DM (n = 32) than in non-DM patients (OR 4.92; 95% CI 1.53,14.3, $p=0.005$).

Conclusion Twenty-five percent of all DM cases were undiagnosed at the time of AAA surgery. Based on post-hoc analyses, undiagnosed DM seems to be associated with an increased risk of organ related complications following

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AAA surgery. This study suggests universal DM screening in AAA patients to reduce the number of DM patients being undiagnosed and to improve proactive diabetes care in this population. The results from post-hoc analyses should be confirmed in future studies.

Keywords Abdominal aortic aneurysm (AAA), Infrarenal AAA repair, Open surgical aneurysm repair (OSR), Endovascular aneurysm repair (EVAR), Diabetes mellitus (DM)

Background

Progressive enlargement of the abdominal aorta may lead to abdominal aortic aneurysm (AAA) formation and subsequently rupture. Several risk factors are associated with AAA formation, including smoking, family history, male sex, advanced age, atherosclerosis, and hypertension [1]. AAA in patients with diabetes mellitus (DM) is reported to have a slower growth rate and a reduced rupture risk compared to in non-DM patients [2, 3]. However, DM negatively affects life expectancy due to its role in inducing and accelerating atherosclerosis and its complications [4, 5]. A multifaceted approach to medical treatment in patients with DM has been shown to reduce cardiovascular complication rates [6–9]. However, DM may remain asymptomatic and undiagnosed for an extended period, leaving the patients untreated and unaware of their heightened cardiovascular risk [10, 11].

The prevalence of DM is increasing globally [12]. Therefore, the number of AAA patients with DM is expected to rise. In general, patients with DM are considered to have high surgical risk due to possible cardiovascular and DM related complications. To date, studies that have examined the impact of DM on outcome following a AAA repair have been based on registry data and heterogenous AAA populations, and it is undecided if the outcome is worse in DM patients [13–17].

Moreover, a small Norwegian study on glycaemic status and mortality in 66 patients undergoing elective AAA repair reported an elevated mortality rate in patients with DM [18]. Half of the patients with AAA and DM had undiagnosed DM upon admission for AAA surgery. This led to the hypothesis that known and undiagnosed DM might affect outcomes after AAA repair negatively.

Therefore, the aims of this prospective study were to investigate 1). The prevalence of known and undiagnosed DM using HbA_{1c} measurements in patients undergoing elective infrarenal AAA repair; and 2). The effect of DM on perioperative outcome after elective infrarenal AAA open surgical repair (OSR) or endovascular aneurysm repair (EVAR).

Methods

Trial overview and study population

The Norwegian abdominal aortic aneurysm and diabetes (ABANDIA) study is a national prospective multicentre study and comprises 877 patients of Caucasian origin who underwent elective, infrarenal AAA repair (OSR or EVAR) from November 2017 to December 2020 due to degenerative AAA. Eleven out of 15 Norwegian surgical centres collaborated in recruitment and data collection. The exclusion criteria were aneurysms of mycotic, suprarenal, and isolated iliac origin, suprarenal clamping, aortic dissection, and redo-surgery after former infrarenal repair. Initially, 962 patients accepted to participate. Of those, 41 met the exclusion criteria. A further 38 patients were excluded due to missing glycosylated haemoglobin (HbA_{1c}) measurement ($n=4$) or suprarenal clamping ($n=34$). Six patients withdrew consent. Finally, 877 participants were included in the analyses (Fig. 1).

All participants were registered locally at the participating centres and in the Norwegian Vascular Registry (NORKAR). NORKAR is a national person-identifiable health registry. Inclusion in the registry is mandatory for all patients undergoing surgical treatment for vascular disease.

Due to changes in the study management during 2019, in site staffing at several hospitals, and lack of focus on recruitment during the Covid-19 pandemic situation and holiday processing, enrollment in the study was not consecutive. For the same reasons, the planned enrolment-period of 12 months was extended to three years. According to NORKAR, an additional 823 people underwent elective infrarenal AAA repair in the study period but were not recruited for participation in the study.

Data collection

The ABANDIA study used a study-specific research form linked with NORKAR registry data to retrieve and validate baseline data on clinical characteristics, comorbidities, medical treatment (statin, platelet inhibitors/anticoagulants, and antihypertensive medication), and laboratory analyses. Comorbidities registered at baseline included diabetes mellitus, coronary artery disease, cerebrovascular disease, peripheral arterial disease, chronic kidney disease, hypertension, lung disease, and atrial fibrillation and other cardiac arrhythmias. Information on the duration from DM diagnosis to AAA operation was not recorded.

The presented follow-up data covers the in-hospital and the 30-day postoperative periods. Detailed surgical data and information on in-hospital postoperative complications, 30-day reinterventions, and 30-day mortality were extracted from NORKAR and the Norwegian Cause of Death Registry. The registries were linked using the

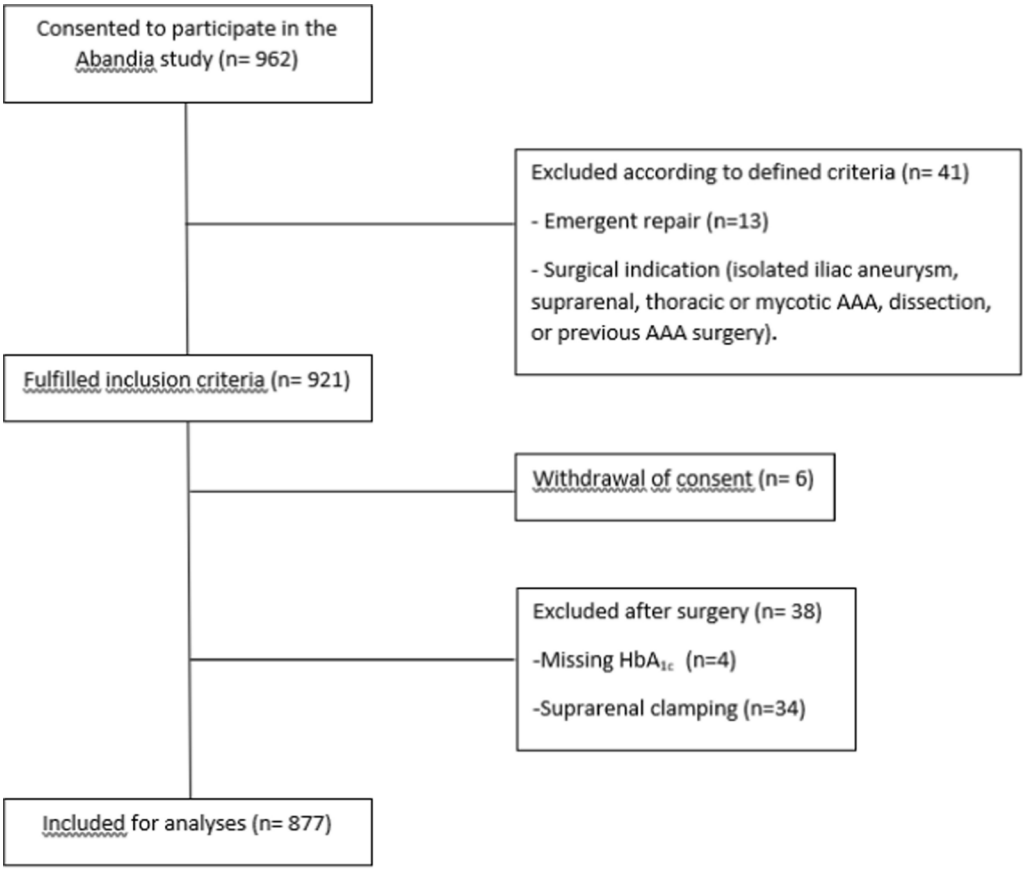

Fig. 1 Flowchart of the Norwegian Abdominal Aortic Aneurysm and Diabetes (ABANDIA) study

participants unique 11-digit Norwegian national identity number. Postoperative complications registered in NORKAR are organ-related (cardiovascular event, cerebrovascular event, renal failure, respiratory failure, multi-organ failure or septicaemia) and procedure-related (graft infection, wound infection, access site complications, haemorrhage, ileus, intestinal ischemia, peripheral embolization, wound dehiscence, compartment syndrome of the extremities, and abdominal compartment syndrome).

Outcomes

The primary outcome measure was the prevalence of previously diagnosed DM and undiagnosed DM detected by HbA_{1c} screening upon admission for AAA repair. DM was diagnosed in accordance with the World Health Organization as $HbA_{1c} \geq 48$ mmol/mol (6.5%). [19].The secondary outcomes were in-hospital complications including organ-failure rates, length of stay, 30-day mortality and reinterventions within 30 days.

Laboratory analyses

Glycosylated haemoglobin (HbA_{1c}) measurements

HbA_{1c} was measured in samples of venous whole blood drawn in tubes containing the anticoagulant ethylenediaminetetraacetic acid (EDTA) and analysed using the following resources: Tosoh G8, G11 or PPLC (Tosoh Bioscience), Sebia (Bergman Diagnostica), and D-100 or Variant II (BioRad). The range of the coefficients of variation of the equipment used for HbA_{1c} measurements was < 3.0% at HbA_{1c} levels 35 mmol/mol (5.4%) and 75 mmol/mol (9.0%). External quality assessment of all equipment used for HbA_{1c} analysis was performed by NOKLUS, a Norwegian national institution certified by The National Institute of Technology (NS-EN ISO 9001:2000).

Biomarkers of renal function

The CKD EPI Equation was used for estimating glomerular filtration rate (GFR) [20].

Statistical analyses

Baseline differences between DM and non-DM patients were evaluated using the *t*-test for continuous variables and the Chi-squared test for categorical variables. Estimates of DM prevalence were reported using counts and percentages, along with 95% confidence intervals (CIs). The CIs were calculated using Wilson's (score) method.

To estimate the effect of DM on risk of complications, adjusted and unadjusted logistic regression models were used. The main predictor was a DM diagnosis, and the adjustment variables were age, sex, body mass index (BMI), smoking (never smoker, previous smoker, current smoker), comorbidity summary, best medical treatment (yes vs. no), and type of operation (OSR vs. EVAR). In accordance with international vascular guidelines, best medical treatment (BMT) was defined as a combination of statin, platelet inhibitor or anticoagulant therapy and antihypertensive medication [21]. The variables included in the multivariate analyses were predefined based on clinical judgement and known clinical risk factors related to a poor outcome after AAA repair [22].

Age and BMI were believed to possibly have a non-linear effect on the outcomes; therefore, these continuous variables were included as restricted cubic splines with 3 knots (placed at the 0.1, 0.5 and 0.9 quantiles). Due to the small number of events, the number of predictors we could include was limited. Comorbidity was therefore included as a summary variable counting the number of comorbidities: coronary disease, cerebrovascular disease including transient ischemic attack, known peripheral vascular disease, lung disease, reduced renal function, atrial fibrillation, and other arrhythmias.

To estimate the effect of DM on length of stay, Cox regression models were fitted with the same predictors as in the logistic models. Deaths before discharge were treated as censored observations. Due to the small number of deaths, the association between diabetes and 30-day mortality was only tested using Fisher's test with mid-*P* correction.

There were very little missing data, and a complete case analysis was therefore used for all statistical models. The significance level was set to $p=0.05$, and all reported CIs are 95% CIs. Calculations for demographics and other patient characteristics were performed using IBM SPSS statistics, version 26 [23]. The other statistical analyses were performed using R version 4.2.3 [24] and the R packages 'rms', 'coin' and 'prodlim' versions 6.7–0, 1.4–2, and 2023.03.31, respectively.

Table 3 Post-hoc multiple logistic regression for predicting organ-related complications, with separate comorbidity variables and DM status split into three groups ($n=854$)

Characteristic	OR	95% CI	*p value*
Age (non-linear effect)	-	-	0.06
Female sex	2.03	0.99, 4.03	0.05
BMI (non-linear effect)	-	-	0.09
Smoking			
Never smoker	-	-	
Previous smoker	0.97	0.38, 3.01	0.95
Current smoker	0.83	0.29, 2.79	0.75
Best medical treatment	1.17	0.63, 2.15	0.62
Type of surgery: EVAR	0.12	0.05, 0.26	< 0.001
Comorbidity			
Cardiovascular disease	0.96	0.51, 1.80	0.90
Lung disease	3.29	1.80, 6.07	< 0.001
Kidney disease	1.81	0.86, 3.64	0.11
Arrythmia	1.31	0.58, 2.76	0.50
Diabetes			0.03
None	-	-	
DM (not previously known)	4.92	1.53, 14.3	0.005
DM (previously known)	0.82	0.23, 2.23	0.73

OR = Odds ratio. CI = Confidence interval

Post-hoc tests

A post-hoc modified logistic regression analysis was performed to examine if any specific *type* of comorbidity was more strongly related to organ-related complications than other types, and if *newly diagnosed* DM was associated with these complications. Results are reported in Table 3, and details are reported in the supplemental material.

Results

Patient characteristics

Baseline characteristics are presented in Table 1. The OSR to EVAR ratio was 52% versus 48% in the total study population, and 54% versus 47% in the DM group. In 777 (88.6%) of the participants, the aneurysm diameter was larger than the recommended threshold for repair (≥5.5 cm in male patients and ≥5.0 cm in female patients). Due to saccular aneurysm, rapid aneurysm growth, coexistent iliac aneurysm or the surgeon's personalized professional decision, aneurysm repair was performed in 68 male patients (7.8%) having an aneurysm diameter between 5.0 and 5.4 cm, and in thirty-four (3.9%) patients having aneurysms 4.9 cm or smaller. Patients with DM had a significantly higher prevalence of cardiovascular comorbidity, higher BMI, were more likely to be male sex and more likely to receive preoperative BMT than non-DM patients. No differences in age, aortic diameter, type of surgical intervention, smoking status, or renal function were registered between the groups. Baseline characteristics were similar in patients with undiagnosed DM as in patients with known DM (Supplementary Table S1). Patients with undiagnosed DM had higher HbA_{1c} and BMI, and were more likely to have a history of coronary artery disease than patients without DM (Supplementary Table S1).

A comparison of baseline characteristics, comorbidities, and medical treatment between the ABANDIA study group and the 823 people not included in the study, is presented in Table S2 and S3 respectively.

Table 1 Baseline characteristics of 877 patients with or without Diabetes following open surgical or endovascular abdominal aortic aneurysm repair.

Characteristics	All patients (n = 877)	No-Diabetes (n = 748)	Diabetes (n = 129)	*p value* [a]
Age—years	73.3 (7.0) [51–94]	73.4 (7.1) [52–94]	72.7 (6.5) [51–88]	0.283
Gender				0.005
Female	142 (16.2)	132 (17.6)	10 (7.8)	
Male	735 (83.8)	616 (82.4)	119 (92.2)	
BMI—kg/m	26.9 (4.2) [15.9–45.5]	26.5 (4.1) [15.9–42.9]	28.7 (4.3) [17.6–45.5]	< 0.001
Missing	*3 (0.3)*	*3 (0.4)*	*0*	
HbA_{1c}—mmol/mol	40.6 (7.6) [20–135]	38.6 (3.7) [20–47]	52.4 (12.3) [32–135]	< 0.001
Total cholesterol—mmol/L	4.2 (1.0) [1.3–8.6]	4.2 (1.0) [1.3–8.6]	3.8 (0.9) [1.4–6.6]	< 0.001
Missing	*39 (4.4)*	*35 (4.7)*	*4 (3.1)*	
LDL cholesterol—mmol/L	2.5 (0.97) [0.7–6.9]	2.6 (1.0) [0.7–6.9]	2.2 (0.8) [0.8–4.9]	< 0.001
Missing	*49 (5.6)*	*44 (5.9)*	*5 (3.9)*	
HDL cholesterol—mmol/L	1.3 (0.4) [0.4–4.1]	1.3 (0.4) [0.4–4.1]	1.2 (0.4) [0.6–2.6]	0.001
Missing	*65 (7.4)*	*58 (7.8)*	*7 (5.4)*	
Aortic diameter—cm	58.4 (7.8) [31–120]	58.2 (7.8) [31–120]	59.3 (7.9) [42–103]	0.177
Surgical intervention				0.755
Open repair	458 (52.2)	389 (52.0)	69 (53.5)	
Endovascular repair	419 (47.8)	359 (48.0)	60 (46.5)	
Smoking status				0.477
Non-smoker	113 (13.1)	99 (13.5)	14 (10.9)	
Former smoker	539 (62.5)	453 (61.6)	86 (67.2)	
Current smoker	211 (24.4)	183 (24.9)	28 (21.9)	
Missing	*14 (1.6)*	*15 (2.0)*	*1 (0.8)*	
Renal function				0.405
eGFR ≥ 60	670 (76.4)	571 (76.3)	99 (76.7)	
eGFR 30–60	192 (21.9)	166 (22.2)	26 (20.2)	
eGFR < 30	15 (1.7)	11 (1.5)	4 (3.1)	
Missing	*0*	*0*	*0*	
Medical history of cerebrovascular disease				0.001
No	784 (89.4)	679 (90.8)	105 (81.4)	
Yes	93 (10.6)	69 (9.2)	24 (18.6)	
Missing	*0*	*0*	*0*	
Medical history of coronary artery disease				0.002
No	611 (69.7)	536 (71.7)	75 (58.1)	
Yes	266 (30.3)	212 (28.3)	54 (41.9)	
Missing	*0*	*0*	*0*	
Medical history of peripheral artery disease				0.017
No	764 (87.1)	660 (88.2)	104 (80.6)	
Yes	113 (12.9)	88 (11.8)	25 (19.4)	
Missing	*0*	*0*	*0*	
Antihypertensive medication				0.102
No	238 (27.2)	211 (28.2)	27 (21.3)	
Yes	636 (72.8)	536 (71.8)	100 (78.7)	
Missing	*3 (0.3)*	*1 (0.1)*	*2 (1.6)*	
Statin				0.065
No	199 (22.7)	178 (23.8)	21 (16.4)	
Yes	677 (77.3)	570 (76.2)	107 (83.6)	

Table 1 (continued)

Characteristics	All patients (n = 877)	No-Diabetes (n = 748)	Diabetes (n = 129)	*p value* [a]
Missing	*1 (0.1)*	*0*	*1 (0.8)*	
Anti-platelet/ anticoagulant therapy				0.175
No	204 (23.3)	180 (24.1)	24 (18.6)	
Yes	673 (76.7)	568 (75.9)	105 (81.4)	
Missing	*0*			
Best medical treatment				0.001
No	450 (51.7)	401 (53.9)	49 (38.6)	
Yes	421 (48.3)	343 (46.1)	78 (61.4)	
Missing	*6 (0.7)*	*4 (0.5)*	*2 (1.6)*	

Data are presented as n (%), mean ± standard deviation (SD) and [range]. BMI = body mass index. LDL = low density lipoprotein. HDL = high density lipoprotein. eGFR = estimated glomerular filtration rate calculated by the CKD EPI Equation. Best medical treatment was defined as a combination of statin, antihypertensive medication, and anti-platelet/anticoagulant therapy

[a] The Norwegian Abdominal Aortic Aneurysm and Diabetes (ABANDIA) study

Fig. 2 Prevalence of known and undiagnosed diabetes mellitus (DM) in 877 patients who underwent elective, infrarenal AAA repair (OSR or EVAR) from November 2017 to December 2020. The areas are proportional to the number of patients

Diabetes prevalence

The total prevalence of DM in patients at baseline was 129/877 (15%; 95% CI 13%,17%), of which 32 (25%; 95% CI 18%,33%) were diagnosed at baseline by HbA_{1c} measurements (Fig. 2). A second confirmative HbA_{1c} test was performed in 31 of the 32 (97%) patients. Of the 748 participants without DM at baseline, 166 (22%) had subdiabetes HbA_{1c} levels of 42–47 mmol/mol (6.0–6.4%), and 582 patients (78%) had normal HbA_{1c} < 42 mmol/mol (6.0%) [19, 25].

Mean HbA_{1c} in patients with known DM at baseline was 51.4 mmol/mol (6.9%) [range 32–87 mmol/mol] versus 55.5 mmol/mol (7.2%) [range 48–135 mmol/mol] in those diagnosed by DM screening at baseline ($p = 0.102$).

Outcomes

30-day mortality

The total 30-day mortality rate was 0.6% (5/877); Two of 32 patients (6%) in the newly diagnosed DM group and three of 748 (0.4%) in the non-DM group ($p = 0.03$). No deaths occurred in patients having previously diagnosed DM at baseline. Three of the five deaths were after OSR, and two were after EVAR.

Procedure-related complications and reinterventions within 30 days

A total of 126 procedure-related complications were registered in 76 patients. Forty of the 76 patients (53%) had one procedure-related complication, and 36 (47%) had two or more.

The number of patients with procedure-related complications requiring reintervention within 30 days postoperatively was 44/76 (58%): Eight (6%) in the DM group versus 36 (5%) in the non-DM group. Of the 44 patients, 27 (61%) had 1 reintervention, and 17 (39%) had 2 or more.

In-hospital organ-related complications

A total of 66 organ-related complications occurred in 58 (7%) patients, of which 10 patients were in the DM group (7.8%) versus 48 patients in the non-DM group (6.4%).

Length of stay

The median length of stay in hospital was five days [0–63], both for DM [0–16] and non-DM [0–63] patients. In patients treated with EVAR, the median length of stay was two days [0–63], compared to seven days [0–36] in the OSR group.

Association of DM with outcomes

Diabetes mellitus was not statistically significantly associated with a higher risk of organ-related complications, procedure-related complications, or length of stay (Table 2). High number of comorbidities, low BMI, being female and open surgical repair were indicative of a higher risk of organ-related complications (Table S4).

According to post-hoc-analyses, the odds of organ-related complications were three times as large (OR 3.29, 95% CI 1.80,6.07, $p<0.001$) in patients with lung disease, and five times as large (OR 4.92, 95% CI 1.53,14.3, $p=0.005$) in patients with newly diagnosed DM than in non-DM patients (Table 3).

Other predictors

The most important predictors of organ-related complications were OSR and the presence of lung disease (Table 3). OSR was the only statistically significant predictor for procedure-related complications (Table S5).

Discussion

The ABANDIA study is a large prospective, multicentre trial comparing the outcome after elective infrarenal AAA repair in patients with or without DM, with comprehensive DM screening at baseline. The total prevalence of DM was 15%. Twenty-five percent of the DM patients were undiagnosed at baseline. No statistically significant association with increased risk of complications, mortality, or longer length of stay in the perioperative period (≤30 days) was found in patients with DM. However, post-hoc analyses indicate that patients with undiagnosed DM are at increased risk of organ-related complications compared to non-DM patients.

Diabetes prevalence

Retrospective European studies report a DM prevalence in surgically treated AAA ranging from 12% in the EUROSTAR registry to 24% in France reported by Raffort et al [13, 15, 26, 27]. In Norway, the DM prevalence in the general population is reported to be 5–12% when based on HbA_{1c} values [28–30]. The highest DM prevalence is found in males, those with obesity, and with advancing age. Hence, the results from this study are comparable to that of the age-matched general Norwegian population.

Globally, it is estimated that 45% of all DM cases are undiagnosed [31]. In Europe, the estimate is 20–30% [31]. In comparison, the proportion of undiagnosed DM cases in the general Norwegian population has been reduced substantially in the last few years and is now estimated to be at 11% compared to 25% in this study [29]. The national Norwegian guidelines' recommendation of HbA_{1c} screening in high-risk individuals may account for this lower proportion of undiagnosed DM in the general population. Although AAA patients often have cardiovascular comorbidities, the vascular surgery guidelines in the USA and in Europe do not address screening for DM in AAA patients [21, 22, 32]. Thus, the high proportion of undiagnosed DM in this study compared to that in the general Norwegian population may be a result of a generally low focus on DM screening in AAA patients.

Complications

Mortality, reintervention, and complication rates were low in this study regardless of DM status. This is in accordance with a contemporary Swedish national study reporting a 30-day mortality rate of 0.9% [33]. Several explanations may account for the low mortality, reintervention, and complication rates in the present study. All primary interventions were performed in an elective setting, and elective AAA repair is reported to have lower mortality rates than acute repair [34]. In addition, only infrarenal AAAs of degenerative origin were included in

Table 2 Logistic and Cox regression analyses of the effect of diabetes on outcome following infrarenal open surgical or endovascular abdominal aortic aneurysm repair in 877 patients*

Outcome	Unadjusted			Adjusted**		
	Estimate	95% CI	*P*-value	Estimate	95% CI	*P*-value
Procedure-related complications, OR	1.48	0.79–2.63	0.20	1.44	0.73–2.68	0.27
Organ-related complications, OR	1.23	0.57–2.39	0.57	1.40	0.62–2.91	0.39
Length of stay, HR	1.06	0.88–1.28	0.54	1.08	0.89–1.32	0.42

* The number of observations in the model varies from 852 to 877 (97%–100%)

** Adjusted for age, sex, body mass index, smoking status, history of coronary artery disease, history of cerebrovascular disease, history of peripheral artery disease, renal function, best medical treatment, and type of surgical repair. See Supplemental Tables S1 and S2 for details on effects estimates for these adjustment variables

CI = confidence interval; OR = odds ratio; HR = hazard ratio

this study. Studies that include AAA of complex origin or suprarenal aortic clamping during OSR report a higher 30-days mortality [33, 35, 36].

Association of DM with complications

DM was not associated with an increased risk of 30-day mortality, reintervention, or in-hospital complications, contrary to what is generally reported [4, 5]. In AAA patients, studies report ambiguous findings; Leurs et al. reported increased 30-day mortality rates in patients with DM following planned EVAR [13]. This is in accordance with a meta-analysis from 2014 reporting a lower perioperative survival rate in AAA patients with DM [16]. However, Hughes et al. found no differences in mortality [14], and Lopez-de-Andres et al. found that elderly type 2 DM patients had significantly lower mortality following AAA repair (OSR and EVAR) than non-DM patients [27].

Perioperative mortality rates were higher around the year 2000 than they are today [13, 14]. In more recent studies, mortality rates following infrarenal AAA repair are generally low, in some instances less than 1% [33, 37]. An increased uptake of EVAR, technical developments, a higher proportion of patients on BMT, and improved DM diagnostics may have positively influenced the outcome following AAA repair. In this study, patients with DM were more likely to receive best medical treatment compared to non-DM patients which is in accordance with DM guidelines [38]. A more optimal medical treatment may be reflected in the findings of lower low-density lipoprotein (LDL) levels in the DM patients. Also, the preoperative mean HbA_{1c} in the DM patients were 52 mmol/mol (6.9%), which is in accordance with general treatment goals according to the DM guidelines [39–41]. De Martino et al. showed that anti-platelet and statin use was associated with improved 5-year survival in patients having coronary risk factors and undergoing AAA repair compared to patients on neither medication [42]. The impact on short-term morbidity and mortality after AAA repair of increasing proportions of patients receiving best medical treatment is still unclear. In addition, with low mortality regardless of type of repair, high numbers of operations would be needed to be able to demonstrate a possible significant difference in mortality between patients with and without DM.

Furthermore, undiagnosed DM was not considered in the mortality and morbidity analyses of the above-mentioned studies [13, 14, 33, 37]. Hence, the significance of undiagnosed DM for postoperative morbidity and mortality was not investigated in those studies.

Association of undiagnosed DM with complications

Results from this study indicate that patients with undiagnosed DM are at increased risk of organ-related complications following AAA repair compared to non-DM patients. To reduce the risk of diabetes-related cardiovascular complications, DM guidelines emphasise the importance of DM screening in high risk individuals, and the use of best medical treatment [38]. AAA patients may be considered high risk individuals due to their high burden of cardiovascular comorbidities, obesity, and high age.

The negative impact of undiagnosed DM has been reported in percutaneous coronary intervention [43] but has not been examined in patients with AAA. However, retrospective cohort studies suggest that hyperglycaemia in patients with and without DM following aortic and non-cardiac surgery may be an indicator of poor clinical outcome [44, 45]. This study was not designed to investigate which pathophysiological mechanisms might be involved in increased risk of peri-operative organ-related complications in patients having undiagnosed DM. However, one could speculate that a metabolic dysregulation and the lack of stabilising DM medication may be involved.

Strengths and limitations

The strength of this study is its prospective multicentre design, with national-level data on elective AAA surgeries from 11 of 15 vascular surgery units in Norway. The study included both OSR and EVAR. In general, studies exploring and comparing outcome following AAA repair in patients with and without DM are often retrospective, registry-based and include a heterogenous study population. In this study, only patients admitted for elective, degenerative infrarenal AAA repair, were included. Hence, the study population was homogeneous and well defined.

The guidelines for DM recommend confirmatory testing in asymptomatic individuals if a screening test is positive [46]. A second, and confirmative, HbA_{1c} measurement was made in 97% of the study population with screening-detected DM, minimizing the risk of misdiagnosing DM patients.

During the study period (December 2017–December 2020), a change of principal investigator due to terminal disease, employment-related changes in site staffing at several study sites, and lack of focus on recruitment during the Covid-19 pandemic situation and holiday processing, affected recruitment into the study. The enrolment has, for this reason, not been consecutive, leading to a reduced participation rate.

Even though the sample size is not small ($n=877$), the confidence intervals for ORs and HRs in the regression models are wide enough to also include clinically significant effect size. The association of undiagnosed DM (n=32) with organ-related complications was evaluated using a post-hoc modified logistic regression analysis. Hence, results should be seen as hypothesis generating

and confirmed in future studies. Due to the low number of deaths, we had low statistical power (i.e., large risk of type II error) for this outcome. Hence the association between DM and 30-day mortality should be interpreted with caution, and further explored. Potential underreporting of complications cannot be excluded since complications were reported by the treating vascular surgeon.

Conclusions

This study represents a large prospective, multicentre trial investigating the prevalence of known and undiagnosed DM, and its impact on outcomes following elective infrarenal AAA repair, with comprehensive DM screening at baseline. The total prevalence of DM was 15%, of which 25% of the DM cases were undiagnosed upon admission for AAA repair.

DM was not statistically significantly associated with an increase in 30-day mortality rate or postoperative complications including 30-day reinterventions. However, based on post-hoc analyses, undiagnosed DM seems to be associated with an increased risk of perioperative organ related complications following AAA surgery. The results from post-hoc analyses should be confirmed in future studies.

We suggest implementing universal DM screening in AAA patients to reduce the number of patients with undiagnosed DM, which may improve proactive diabetes care in this population.

Abbreviations

AAA	Abdominal Aortic Aneurysm
ABANDIA	Abdominal aortic Aneurysm and Diabetes
BMI	Body mass index
BMT	Best Medical Treatment
CI	Confidence interval
DM	Diabetes Mellitus
EDTA	Ethylenediaminetetraacetic acid
EVAR	Endovascular aneurysm repair
GFR	Glomerular filtration rate
HbA_{1c}	Glycosylated haemoglobin
HR	Hazard ratio
LDL	Low-density lipoprotein
NORKAR	Norwegian Registry for Vascular Surgery
OR	Odds ratio
OSR	Open surgical aneurysm repair

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12933-024-02421-w.

Additional file1 (PDF 268 kb)

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Author contributions

JW, MV:Analysis and interpretation, writing the manuscript, critical revision, approval of the manuscript, and agreement to be accountable. TB: Analysis and interpretation, data collection, writing the manuscript, critical revision, approval of the manuscript, agreement to be accountable and obtaining funding. KH, LN: Analysis and interpretation, statistical analysis, writing the manuscript, critical revision, approval of the manuscript, and agreement to be accountable. MA, MH, HL, HF, IS, BW, CL, EP, IK, EG, SK: data collection, critical revision, approval of the manuscript, and agreement to be accountable. EM, TJ:Conception and design, analysis and interpretation, writing the manuscript, critical revision, approval of the manuscript, and agreement to be accountable. IH:Conception and design, data collection, analysis and interpretation, statistical analysis, writing the manuscript, critical revision, approval of the manuscript, agreement to be accountable and obtaining funding.

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Availability of data and materials

The data that support the findings of this study are available from Haukeland University Hospital, Bergen, Norway, but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and if permission from each of the participating research sites is granted.

Declarations

Ethics

The study was approved by the Regional Committee for Medical Research Ethics (REK Vest 2017/1183) and registered in Cristin, the national research information system of Norway. Informed written consent was obtained from all participants. The study was conducted according to the principles of the Declaration of Helsinki.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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