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Review Article

CLINICAL PRACTICE

Diabetes mellitus and perioperative outcomes: a scoping review of the literature

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Abstract

Background: Diabetes mellitus (DM) is frequently encountered in the perioperative period. DM may increase the risk of adverse perioperative outcomes owing to the potential vascular complications of DM. We conducted a scoping review to examine the association between DM and adverse perioperative outcomes.

Methods: A systematic search strategy of the published literature was built and applied in multiple databases. Observational studies examining the association between DM and adverse perioperative outcomes were included. Abstract screening determined full texts suitable for inclusion. Core information was extracted from each of the included studies including study design, definition of DM, type of DM, surgical specialties, and outcomes. Only primary outcomes are reported in this review.

Results: The search strategy identified 2363 records. Of those, 61 were included and 28 were excluded with justification. DM was mostly defined by either haemoglobin A1c (HbA1c) or blood glucose values (19 studies each). Other definitions included 'prior diagnosis' or use of medication. In 17 studies the definition was unclear. Type 2 DM was the most frequently studied subtype. Five of seven studies found DM was associated with mortality, 5/13 reported an association with 'complications' (as a composite measure), and 12/17 studies found DM was associated with 'infection'. Overall, 33/61 studies reported that DM was associated with the primary outcome measure.

Conclusion: Diabetes mellitus is inconsistently defined in the published literature, which limits the potential for pooled analysis. Further research is necessary to determine which cohort of patients with DM are most at risk of adverse postoperative outcomes, and how control influences this association.

Keywords: blood glucose; complications; diabetes mellitus; glycated haemoglobin; postoperative complications; scoping review

Editor's key points

- Diabetes mellitus is widely considered to be a risk factor for adverse postoperative outcomes, but it is not known whether this is true for all patients with diabetes mellitus.
- Diabetes mellitus is inconsistently defined in the literature and available studies report mixed associations between diabetes mellitus and postoperative outcomes.
- More work is warranted to identify the cohort of patients with diabetes mellitus most at risk of adverse outcomes by examining factors such as control of blood glucose.

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Diabetes mellitus (DM) is frequently encountered perioperatively. Operations in patients with DM account for 15% of all procedures. Furthermore, up to 50% of patients with DM will require a surgical procedure during their lifetime.[1,2] DM is largely divided into two main categories: type 1 DM (absolute insulin deficiency) and type 2 (insulin resistance and relative insulin deficiency),[3] whereas in a minority diabetes is attributable to secondary causes, such as endocrine conditions and steroid use, or genetic disorders, including maturity onset diabetes of the young. However, the different types of diabetes are often discussed as a single entity and referred to as 'diabetes'. This has the potential to cause confusion when developing guidelines for clinical practice.[4] For example, guidelines mandating minimum fluid infusion rates have the potential to cause harm with respect to a patients' overall fluid balance. To exemplify this, consider the patient with DM after major surgery who requires a variable rate insulin infusion for their glucose control, intravenous fluids with their patient-controlled analgesia system, an epidural infusion, and total parental nutrition. There are several insulin infusion regimes in use in current clinical practice, many of which evolved from research by Alberti and Thomas[5] in the 1970s. Although there is solid clinical reasoning to use such methods for patients with type 1 DM, and in certain situations for patients with type 2 DM, developing and instigating guidelines requires careful consideration.

The long-term sequelae of poor glycaemic control in DM are increased risk of microvascular and macrovascular complications.[3,6] A key concern for patients with DM undergoing surgery is increased risk of infection, which is thought to be secondary to modulation of immune response pathways.[7] Postoperative complications such as infection can result in longer lengths of stay, higher re-admission rates, and inferior surgical outcome.[8] Therefore, current guidelines focus on the association between poor glycaemic control in DM (defined as glycated haemoglobin A1c [HbA1c] >69 mmol L^{-1} or 8.5%) and adverse surgical outcomes.[9,10] This has the potential to cause further confusion when studying this area – are all patients with DM at equal risk, or is glycaemic control the crucial factor? There is some evidence that if the diagnosis of DM is known before surgery, outcomes may be better.[9] The current narrative is that DM is a risk factor for poor postoperative outcome, although no formal review has been undertaken in the noncardiac surgery literature to explore this concept.

Given the observational nature of this question and the heterogeneity of outcomes, it was decided that a scoping

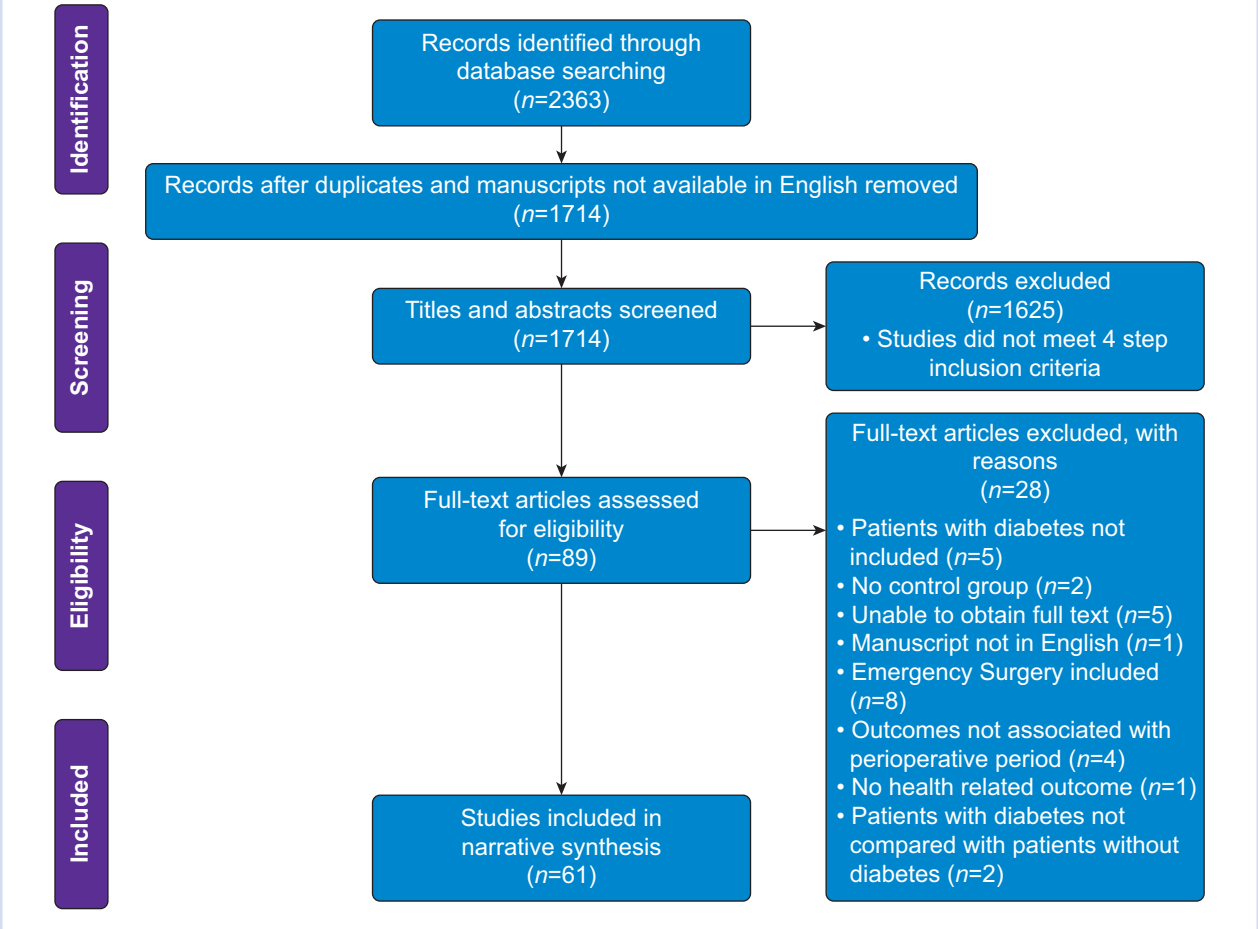

Fig 1. PRISMA flowchart demonstrating the full scoping review process from initial search to abstract screening and full text assessment. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

Table 1 Summary of all papers included in the review. Data are grouped according to their primary outcome measure. *Not reported. AVf, arterio-venous fistula; CI, confidence interval; DM, diabetes mellitus; HD, haemodialysis; HR, hazard ratio; IGT, impaired glucose tolerance; IOP, intraocular pressure; IPTW, inverse probability of treatment weighting; JOA, Japanese Orthopaedic Association (Changes in motor, sensory and bladder function); LOS, length of stay; OR, odds ratio; PJI, prosthetic joint infection; QuickDASH, Quick Disabilities of the Arm, Shoulder and Hand (patient reported outcome measure assessing disability); RR, relative risk; SD, standard deviation; SSI, surgical site infection; UTI, urinary tract infection; WOMAC, Western Ontario and McMaster Universities Arthritis Index.

Year	First author	Study design	# Patients (DM)	# Patients (control)	Surgical specialty	Primary outcome measure (mortality)	Reported differences between groups	DM associated with outcome
2014	Guzman[64]	Retrospective cohort	423 050	2 145 944	Spinal	Mortality	OR=1.44; 95% CI, 1.19–1.74; P=0.0001	Yes
2014	Guzman[63]	Retrospective cohort	223 908	1 378 237	Spinal	Mortality	OR=2.08; 95% CI, 1.72–2.50; P<0.0001	Yes
2009	Marchant[62]	Retrospective cohort	109 458	920 555	Orthopaedic	Mortality	Controlled DM *vs* no diabetes: OR=0.855; 95% CI, 0.679–1.076; P=0.182 Uncontrolled diabetes *vs* no diabetes OR=2.700; 95% CI, 1.647–4.426; P<0.001	Yes
2015	Lee[54]	Retrospective case-control	419	2656	Urology	All-cause mortality	OR=1.825; P=0.001	Yes
2019	Zarrouk[66]	Retrospective cohort	397	1709	Vascular	Mortality	IPTW adjusted Cox regression (RR=0.98; CI, 0.75–1.29; P=0.91)	No
2019	Long[44]	Retrospective cohort	261	790	Vascular	30-day mortality	DM: 2.5% Control (glucose >180 mg dl^{-1}): 8.5% (P=0.02)	No
2016	Hjellestad[17]	Prospective cohort study	8	58	Vascular	All-cause mortality	Multivariate Cox regression HR death=6.35; 95% CI, 1.49–27.1; P=0.01	Yes

Year	First author	Study design	# Patients (DM)	# Patients (control)	Surgical specialty	Primary outcome measure (Composite measure of morbidity and mortality)	Reported differences between groups	DM associated with outcome
2019	Wysocki[51]	Retrospective cohort	343	1375	General	Overall morbidity rate	DM: 7.27% Control: 5.58% Pre-diabetes: 6.64%; P=0.571	No
2019	Guetta[45]	Retrospective cohort	143	841	General	Mild complication (Clavien–Dindo classification <3a)	OR=2.32; 95% CI, 1.16–4.6; P=0.017	Yes
2015	Reategui[43]	Retrospective case series	130	703	Orthopaedic	Medical, infectious, mechanical, and surgical complications	–*	No
2015	Goodenough[72]	Prospective cohort	129	888	General	Major complication using (Clavien–Dindo classification system) within 30 days of surgery	OR=1.17; 95% CI, 0.57–2.41; P=0.66	No
2019	Law[23]	Retrospective cohort	104	104	Orthopaedic	Complication rate	DM: 5.8% Control:4.8%	No

Continued

Table 1 Continued

Year	First author	Study design	# Patients (DM)	# Patients (control)	Surgical specialty	Primary outcome measure (Composite measure of morbidity and mortality)	Reported differences between groups	DM associated with outcome
2015	Kallio[69]	Retrospective cohort study	103	100	Orthopaedic	Complication rate	DM (A1c <10%) + referral: 0.78 (1.01) DM no referral: 1.27 (1.18) No DM: 0.36 (0.63) (P=0.124) DM (A1c <8%) + referral: 0.50 (0.89) (P=1)	Yes
2016	Swirska[21]	Retrospective cohort	91	91	Gynaecological	Number of perioperative complications (e.g. UTI, impaired wound healing)	OR=1.83; 95% CI, 0.68−4.96; P=0.24	No
2006	Hofmann[42]	Prospective cohort	80	544	Vascular	Periprocedural complications (fatal and non-fatal stroke, non-fatal myocardial infarction)	Inadequate control (HbA1c >7%) OR=3.7; 95% CI, 1.5−9.1; P=0.005	Yes
2012	Myers[68]	Retrospective cohort	74	74	Orthopaedic	Any complication (infection, non-infection [e.g. non-union])	OR=2.9; 95% CI, 1.42−5.96; P<0.005	Yes
2018	Kamarajah[27]	Prospective cohort study	49	132	General	Overall complications (Clavien−Dindo)	Multivariate logistic regression: OR=2.08; 95% CI, 1.04−3.99; P=0.031	Yes
2020	Law[67]	Retrospective cohort	40	80	Orthopaedic	Overall complication rate (infection, reoperation, non-union)	DM: 17.5% Control: 23.8% (P=0.489)	No
2019	Rudolph[24]	Retrospective cohort	39	112	General	Major complications	DM: 53% (P=0.514)	No
2016	Bianchini[28]	Retrospective cohort	31	137	Head and neck	Postoperative complications	Multivariate logistic regression: OR=1.042; 95% CI, 0.416−2.607; P=0.930	No

Year	First author	Study design	# Patients (DM)	# Patients (control)	Surgical specialty	Primary outcome measure (Infections)	Reported differences between groups	DM associated with outcome
2018	Cancienne[61]	Retrospective cohort	13 470	103 586	Orthopaedic	Deep infection within 6 months requiring debridement	DM: 0.33% Control: 0.19% (P=0.001)	Yes
2019	Lipsky[58]	Retrospective cohort	4478	10 491	Urology	Inflatable penile prosthesis infection	HR=1.32; 95% CI, 1.05−1.66; P=0.016	Yes
2013	Kwon[56]	Retrospective cohort	4098	7532	General	Composite infections	Non-insulin DM: OR=0.51; 95% CI, 0.37−0.69 Insulin DM: OR=0.52; 95% CI, 0.35−0.76	No
2015	Maradit Kremers[59]	Retrospective cohort	3507	16 664	Orthopaedic	PJI	HR=1.23; 95% CI, 0.87−1.74	No
2017	Hoelzer[53]	Retrospective cohort	452	2285	Pain	Infection rate	DM: 1.99% Control: 2.54% (P=0.49)	No

Continued

Table 1 Continued

Year	First author	Study design	# Patients (DM)	# Patients (control)	Surgical specialty	Primary outcome measure (Infections)	Reported differences between groups	DM associated with outcome
2014	Wukich[52]	Prospective cohort	323	1737	Orthopaedic	SSI	OR=3.99 (95% CI, 2.39–6.68)	Yes
2011	Wukich[49]	Prospective cohort	221	1241	Orthopaedic	SSI (within 30 days)	DM: 9.5% Control: 2.4% (P<0.00)	Yes
2017	Rahimi-Nedjat[50]	Retrospective cohort	120	1254	Maxillo-facial	Infections	DM: 15.0% Control: 12.1% (P=0.383)	No
2014	Fisichella[33]	Retrospective case-control	111	176	Orthopaedic	SSI	OR=8.7	Yes
1984	Vannini[48]	Retrospective cohort	47	1180	Orthopaedic	Deep phlagosis (infection)	DM: 11% Control: 2% (P<0.001)	Yes
2020	Keavy[39]	Retrospective cohort study	43	321	Gynaecological	Infection	DM: 12.4% Control: 7.5% (P<0.05)	Yes
2006	Liao[37]	Retrospective cohort	39	298	Spinal	Infection	DM: 10.3% Control: 0.7% (P=0.003)	Yes
2014	Hikata[38]	Retrospective case-control	36	309	Spinal	SSI	DM: 16.7% Control: 3.2% (P=0.0005)	Yes
2016	Iavazzo[36]	Prospective cohort	34	266	Gynaecological	Infective complications	DM: 32.4% (P=0.048)	Yes
2008	Olsen[70]	Retrospective nested case-control	29	199	Orthopaedic	SSI	OR=3.5 (95% CI, 1.2–10.0)	Yes
2013	Motta[13]	Prospective case-control	28	18	Dental	Clinical complications (surgical site infection, systemic infection)	Controlled DM: 7.7% Uncontrolled DM: 13.3% No DM: 5.6%, Fisher's exact test (P=0.81)	No
2010	Ata[65]	Retrospective medical record review	–*	–*	General/vascular	Postoperative infection	Vascular – adjusted OR=1.84 (95% CI, 1.20–2.82) General – adjusted OR=1.80 (95% CI, 1.12–2.90)	Yes

Year	First author	Study design	# Patients (DM)	# Patients (control)	Surgical specialty	Primary outcome measure (specialty Specific)	Reported differences between groups	DM associated with outcome
2013	Adams[60]	Retrospective cohort	7567	32 924	Orthopaedic	Revision arthroplasty	HbA1c <7%, OR=1.32 (95% CI, 0.99–1.76) HbA1c >7%, OR=1.03 (95% CI, 0.68–1.54)	No
2013	Takahashi[26]	Retrospective cohort	41	124	Spinal	JOA score	DM: 22.7 (SD 5.6) Control: 24.4 (SD 4.2) (P=0.137)	No
2000	Kawaguchi[14]	Retrospective case-control	18	34	Spinal	JOA score	DM: 12.6 (2.0) Control: 13.3 (2.1) (P=0.25)	No
2012	Dokai[19]	Retrospective case series	13	65	Spinal	JOA score	DM: 12.1 (7–16.5) Control: 12.4 (6.5–17) (P=0.578)	No
2017	Brock[22]	Retrospective matched cohort	100	100	Orthopaedic	WOMAC scores (pain, stiffness, and physical function)	–*	Yes
2018	Moazzeni[16]	Prospective case-control	48	48	Spinal	Rate of Fusion at 1 yr	DM: 58% Control: 79% (P=0.02)	Yes
2018	Sun[29]	Retrospective case-control	11	141	Orthopaedic	New onset or exacerbation of nerve symptoms	DM: 27% Normal glucose tolerance: 9% Impaired regulation: 19% (P=0.112)	No

Continued

Table 1 Continued

Year	First author	Study design	# Patients (DM)	# Patients (control)	Surgical specialty	Primary outcome measure (specialty Specific)	Reported differences between groups	DM associated with outcome
2019	Singh[30]	Prospective cohort	150	150	Ophthalmic	Eye Complications (transient corneal oedema)	–*	No
1993	Kodama[34]	Retrospective cohort	36	184	Ophthalmic	Ophthalmic Complications (Macular Oedema and Transient elevation of intraocular pressure)	IOP; DM: 13%, Control 4% Oedema; DM: 18%, Control 2% ($P<0.05$)	Yes
2013	Law[18]	Retrospective case-control	29	64	Ophthalmic	Rate of qualified surgical success (IOP <15 and >5 mm Hg, without complications)	DM: 61% Control: 64.2% ($P=0.881$)	No

Year	First author	Study design	# Patients (DM)	# Patients (control)	Surgical specialty	Primary outcome measure (Other including cardiovascular, renal, and LOS)	Reported differences between groups	DM associated with outcome
2014	Underwood[46]	Retrospective cohort	449	888	General/vascular	LOS	DM: 6. (6.6) Control: 5.2 (5.3); $P<0.0001$	Yes
2018	Lenguerrand[40]	Prospective cohort	64	523	Orthopaedic	LOS	DM: 5 days Control: 4 days ($P=0.3$)	No
2019	Villamiel[25]	Retrospective cross-sectional	44	113	General	LOS	T2DM: 5.8 (SD 3.8) Control: 6.4 (SD 5.1); $P=0.476$	No
2013	Bakker[47]	Retrospective cohort	329	1133	Vascular	30-day cardiovascular complications	OR=1.80; 95% CI, 1.24–2.61; $P<0.01$	Yes
2011	Biteker[71]	Retrospective cohort	204	344	Mixed	Perioperative cardiovascular events (PCEs)	DM: 24.5% IGT: 9.8% Control: 5% ($P<0.001$)	Yes
2017	Shin[73]	Retrospective cohort	6034	48 811	Spinal	Acute renal failure	OR Controlled DM 1.863; 95% CI, 1.35–2.58; $P<0.05$ OR Uncontrolled DM 4.84; 95% CI, 1.75–13.39; $P<0.05$	Yes
2008	Feringa[35]	Retrospective cohort	69	220	Vascular	Ischaemic Events	OR=2.6 (95% CI, 1.4–4.9)	Yes
2012	Afsar[32]	Retrospective cohort	73	160	Vascular	Failure of AVF before first HD session	DM HbA1c >7%: 52.8% DM HbA1c <7%: 29.7% Control: 27.5% ($P=0.013$)	Yes
2020	Reinstatler[20]	Retrospective cohort	92	81	Urology	30-day postoperative visits for pain (ED or clinic)	–*	No
2011	Hwang[31]	Retrospective cohort	92	159	Urology	Recurrence free survival in months	Kaplan–Meier: HR=2.11; 95% CI, 1.4–3.2; $P=0.001$	Yes
2020	Chung[41]	Retrospective cohort	67	538	Urology	Post-void residual volume at 3 months (ml)	DM: 30.6 (41.3) Control: 47.6 (89.4); $P=0.306$	No
2018	Schroer[55]	Retrospective cohort	237	6107	Orthopaedic	Mean 90-day charges	$5074 increase in cost	Yes
2019	Zimmerman[57]	Retrospective cohort	1503	9139	Plastic	QuickDASH score	DM: 25 Control: 27 ($P=0.263$)	No
2008	Tawil[15]	Prospective case-control	45	45	Dental	Implant survival	–*	No

review would be the best way to systematically map the literature to guide development of robust observational research in this area. Our scoping review is based on the following research question: Does existing literature support that DM is an independent risk factor for adverse perioperative outcomes?

We also explored the way DM is defined in the published literature and the current understanding of the relationship of control (defined by HbA1c level) and outcomes.

Methods

This scoping review was performed in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, extended for use with scoping reviews.[11] The protocol was developed before commencing the review and is available upon request from the corresponding author.

Literature search

An initial scoping search was performed using PubMed to collate relevant keywords and medical subject headings (MeSH). These were collated into a systematic search strategy combining free text and Boolean logic terms. The search was applied in CINAHL, the Cochrane library, MEDLINE, SCOPUS, and Web of Science. An example search strategy can be found in Appendix 1. The initial search strategy was developed with the assistance of an experienced Information Scientist (NK) in accordance with best practice guidelines.[11] Reference lists of included studies and relevant reviews were also searched to supplement the systematic search. Where full texts were not available, we contacted the authors, which was successful in one case.

Eligibility criteria

The review question was specifically designed to address the epidemiology of outcomes for patients with DM and therefore studies investigating an intervention, such as RCTs, were excluded. Only manuscripts covering health-related outcomes, including patient-reported outcomes, were included. It was a prerequisite that papers included patients with and without DM undergoing elective, noncardiac surgery. We further limited the search to adult patients as the epidemiology of DM differs significantly between adult and paediatric patients.

Selection of studies

Duplicate references were removed using EndNote (EndNote, Clarivate Analytics). Manuscripts not available in English were also excluded at this stage. After removal of duplicates, studies were uploaded onto Rayyan (Rayyan Systems Inc. Online Software; available from: https://www.rayyan.ai/).[12] As part of a consistent and comprehensive screening process two authors (DD and RB) screened all titles and abstracts independently to identify relevant studies for full text review. Rayyan collates a list of disagreements between the two authors, which were then examined by a third author (MA) to determine final inclusion.

Data extraction

The full texts identified for review were re-imported to a reference management software (EndNote, Clarivate Analytics). A screening and data collection tool was created *a priori* and tested (DD and RB) on the first 10 papers to assess suitability. All full texts were re-assessed against the key inclusion criteria and then relevant data was extracted using Microsoft Excel (Microsoft Corp., Redmond, WA, USA). Three authors were involved in data extraction (DD, RB, and CDF). Consensus was sought between the three extracting authors in cases of uncertainty. We recorded article characteristics such as design, statistical methods, Definition of DM, type of DM, participant counts, surgery types, and outcomes. Many studies looked at multiple outcomes. When it was not clear which was the primary outcome, we selected the outcome most applicable across different surgical specialities (i.e. mortality).

Data synthesis

Microsoft Excel was used to synthesise extracted data. We grouped studies based on the Definition of DM they used and the outcomes they studied, and value cut-offs for descriptors of glycaemic status. Frequencies were produced for the definitions studied, and we visually displayed these using a bubble plot. All included texts were synthesised into a single table to compare the outcomes studied.

Results

The systematic search produced 2363 records. After duplications had been removed, 1714 title and abstracts were screened and 1625 excluded. The full text of 89 articles was assessed for eligibility. A total of 61 papers were included[13–40,41–73] based on the predetermined criteria (described above). The remaining 28 articles were excluded with the reasons summarised in Fig 1. Table 1 summarises the included papers. Publication date ranged from 1984 to 2020. All studies used observational designs; most were retrospective designs with 12 studies utilising prospective methodologies. The range of patients with DM studied was from 8 to 423 050. The range of control patients was 18–2 145 944. The surgical specialties represented included: dental, spinal, vascular, ophthalmic, orthopaedic, urology, gynaecological, general, head and neck, and maxillo-facial.

Definition of diabetes mellitus used

The definition of DM used varied substantially as illustrated in Fig 2. HbA1c was used in 19 studies. A HbA1c of >6.5% was the most common cut-off applied in five studies. Notably, in one study HbA1c values within the preceding 1–2 yr before study were accepted as diagnostic.[45] In the 19 studies reporting blood glucose, a range of diagnostic methods were reported including random, fasting, and glucose tolerance tests. In one study, diabetes mellitus was self-reported as part of the functional co-morbidity index, which was later corroborated against participants' medications. They found all patients had correctly reported their status but were unable to distinguish between type 1 and type 2 DM.[40] In 17 studies the definition was unclear, or not reported in the manuscript. In six cases, DM was defined by use of hypoglycaemic agents. Three studies specifically referenced international guidelines (WHO and American Diabetes Association).

It was not always clear which type of DM was being studied. Forty studies specified DM, but not which type. Five studies used 'Type 1 and Type 2' to classify DM. In nine studies patients with type 1 DM were excluded, and only type 2 DM was

studied. In one study the registry from which patients were identified contained 98% patients with type 2 DM but the analysis was done using presence *vs* absence of DM.[66] Fourteen studies subclassified DM by control.[13, 15, 32, 39, 40, 42, 43, 52, 55, 62–64, 72, 73] Of these, 11 used HbA1c to define control. Cut-offs included 6.5%, 7%, 8%, 7–9%, 8–9%, and 47 mmol mol^{-1}. The remaining three used International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) codes which are linked with complications (such as ophthalmic manifestations).[62–64] Other ways of subcategorising patients included by management. For example, insulin-*vs* non-insulin-dependent DM was found in four studies. Overall, there was no consistency in the way DM or control of DM was defined.

Outcomes studied

Table 1 outlines the primary outcomes studied. Some studies used outcomes that would be applicable to all surgical specialties (i.e. mortality and length of stay), whereas others used outcomes specific to a surgical speciality (e.g. Japanese Orthopaedic Association [JOA] scores and need for revision arthroplasty). Seven studies analysed mortality and found that DM was associated in five cases. Mortality was analysed within different timescales including: inpatient, 30-day, and longer term (up to 8 yr).[44, 54, 62–64, 66] In one study mortality was included as part of a composite measure ('adverse postoperative outcomes').[73] In 12 studies perioperative complications were analysed as a group, as a composite measure. Patients with DM experienced higher rates of complications in five of these studies. Infection was analysed in 17 studies. Like mortality, infective outcomes were not consistently defined. Definitions of infection included surgical site infection, unrelated infection (such as urinary tract, or pulmonary), and operation specific infection (prothesis infection). Infection was frequently included in composite outcomes. Where it was the primary outcome, DM was associated with postoperative infection in 12 cases.

Of the 60 papers included in this scoping review, 33 reported that DM was associated with their primary outcome measure. Often multiple outcome measures were studied; this meant that DM may have been associated with one outcome, but not another in the same study.[62,63]

Discussion

This scoping review is the first of its type to examine the existing literature studying the relationship between DM and adverse perioperative outcomes in the noncardiac surgery literature. Understanding this relationship is important for guiding future research in this area and identifying where targeted interventions will benefit patients most. This is increasingly important as the burden of DM increases among surgical patients.[74,75]

Variable definition of diabetes mellitus

Through the systematic search of the available literature, we found that DM is defined in multiple ways: using HbA1c values, blood glucose investigations, patient records, and prescribed medications. Furthermore, the cut-offs applied for the Definition of DM, and glycaemic control varied substantially. Such inconsistencies have the potential to undermine

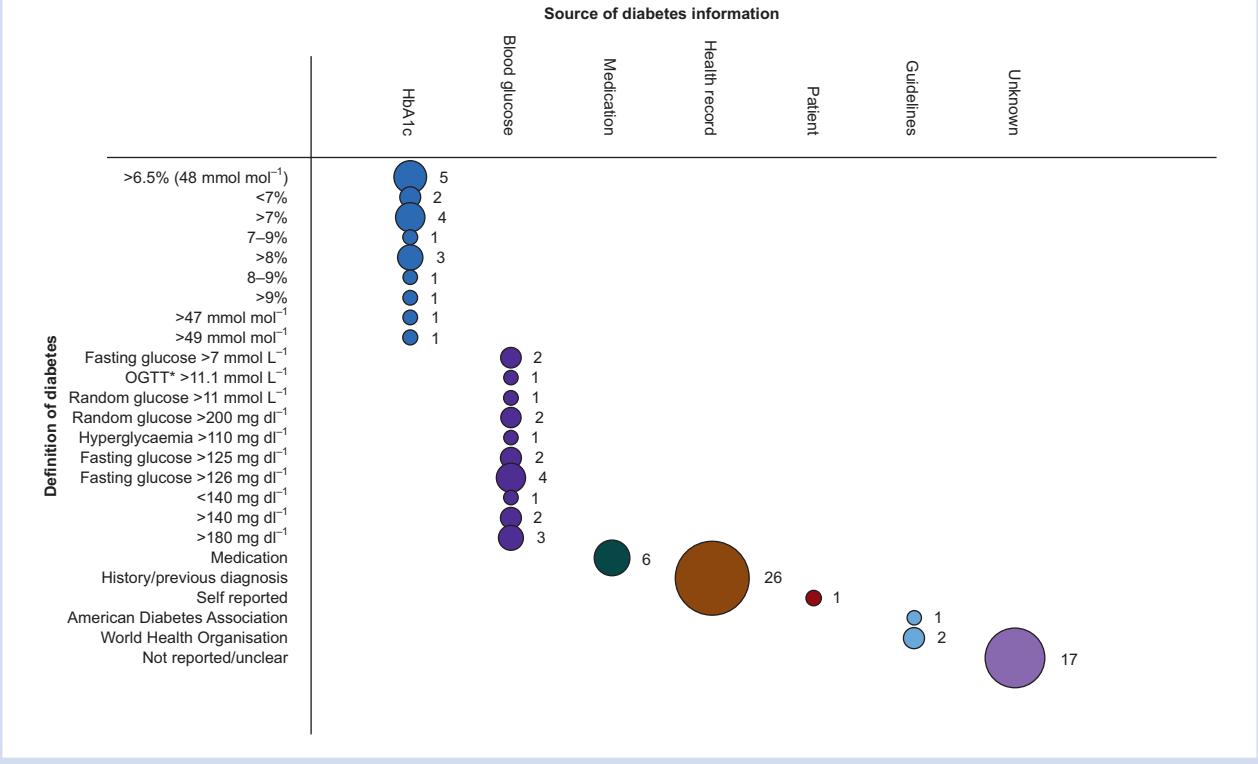

Fig 2. Bubble plot of diabetes mellitus definitions. Bubble plot depicting the range of definitions used in the published literature studying the association between diabetes mellitus and adverse postoperative outcomes. *OGTT, oral glucose tolerance test. HbA1c, haemoglobin A1c.

the value of pooled analyses.[76] It may be possible to perform a systematic review and meta-analysis with the existing literature, but it would require asking a well-formulated question, focusing on just one of the outcome measures such as mortality or infection, which both have studies addressing them with thousands of patients included. However, to take mortality as an example, caution would be necessary as all seven studies from this scoping review used a different definition of DM.

In addition, variable definitions and cut-offs may cause confusion when discussing glycaemic control. This is an important consideration for the perioperative multidisciplinary team who need to communicate with diabetes specialists, support preoperative optimisation, and decide whether it is appropriate to proceed with an operation.[2] The American Diabetes Association have published consensus guidelines advising the use of hyperglycaemia, hypoglycaemia, time in range, and diabetic ketoacidosis as clinically meaningful outcomes measures in type 1 DM, which could be modified for use in type 2 DM.[77]

Limitations of HbA1c

Existing guidelines focus on HbA1c as a marker of glycaemic control.[78] HbA1c gives an average of control over 2–3 months and is widely used because of its low costs and reproducibility of measurement. However, literature studying type 1 DM highlights its limitations, specifically its inability to assess short-term glycaemic variability (GV) and its inability to quantify hypoglycaemic burden. Moreover, HbA1c is inaccurate in patients with anaemia or abnormalities in renal function, both of which are common in surgical patients, limiting the value of HbA1c in this setting.[77,79] Short-term GV, as measured with continuous glucose monitors, was not studied in any of the papers found in this scoping review. Incorporating short-term measures of GV are an important consideration for future perioperative research with a potential role in aiding preoperative optimisation but also improved care during a hospital stay by enabling patient autonomy and closer monitoring for complications such as hypoglycaemia.[79,80] Their utility is currently being explored in the cardiac surgery literature.[81] Numerous alternative novel biomarkers for DM diagnosis, control, and complications are currently being explored. Micro-RNAs are currently being studied as potential biomarkers for the early detection of DM and its associated complications. Although scientific and methodological barriers remain before they can be implemented in clinical practice, they show promise and may be relevant to perioperative practice in the next decade.[82,83]

Outcomes studied

On the question of whether DM is a risk factor for adverse postoperative outcome, the answer is patient, operation, and perioperative outcome specific. This scoping review reports primary outcomes, but most papers studied multiple outcomes and many reported associations with some – but not all – outcomes. Interestingly, the four largest studies (>10 000 patients with DM) found an association between DM and their primary outcome measure. For the remaining studies, no trends were seen between study size and likelihood of a detected association. No further trends were noted between factors such as methodology or DM Definition and outcomes.

The outcomes found in this scoping review can be classified as either (1) generalisable to the whole surgical population or (2) specific to certain surgical specialties. In terms of outcomes relevant to all surgical patients, such as mortality, the literature reports an association in most cases, but not all. Similar mixed findings were reported for length of stay (LOS), infection, and composite complication measures. For specialty-specific measures, no differences were seen between groups in studies using the JOA score, but significant differences were found for ophthalmic and vascular complications, which is unsurprising given the micro- and macro-vascular complications associated with DM. The need for consistent definitions for seemingly dichotomous variables such as mortality has been discussed elsewhere.[76] This review corroborates those observations with studies using various mortality endpoints (in-patient *vs* 30-day mortality). We support the call for standardised endpoints in observational studies.

Role of complications of diabetes mellitus related to outcome

It is important to distinguish between definitions of DM control. Many of the studies included in this review specifically referred to glycaemic control (HbA1c), but well-controlled DM refers to more than just a glycaemic marker such as HbA1c. It may include factors such as blood pressure, weight, or lipid status. Three studies had used ICD-9-CM codes to stratify their groups by control, which include reference to microvascular complications.[62–64] A closer examination of the association between presence of DM complications and perioperative outcomes would be of value in future research. This has been explored by our group in colorectal cancer, suggesting that presence of complications is associated with both postoperative mortality (90-day) and death during the surgical episode.[84]

Conclusions

In conclusion, robust observational studies are warranted to further expand our understanding of the relationship of DM to adverse postoperative outcomes. This will be aided by consistent definitions and considering a wider perspective on DM control, including GV and complication status. Defining cohorts of patients with DM who are most at risk will allow implementation of targeted intervention to improve outcomes.

Authors' contributions

Conceptualisation: DJD, RJB, SH, RA.
Methodology: DJD, RJB, SH, RA.
Formal analysis: DJD, RJB, CDSF, MA.
Investigation: DJD, RJB, CDSF, MA.
Writing of original draft: DJD, RJB.
Writing, review, and editing: DJD, RJB, CDSF, MA, SH, RA.
Visualisation: DJD, RJB.
Supervision: SH, RA.

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Declarations of interest

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bja.2022.02.013.

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