Surgery in older patients with diabetes

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1. RECOMMENDATIONS

Patients could be divided into three groups:

1 patients with known diabetes mellitus prior to hospitalization;
2 patients with a first diagnosis of diabetes mellitus made during their stay, which continues after discharge;
3 patients with hyperglycemia related to hospitalization or surgery: they are non-diabetic individuals with hyperglycemia that appears for the first time during hospitalization but does not persist after discharge.

For these patients the suggested actions are:

• To assess the risk-benefit ratio of the surgical procedure in relation to the patient's age, comorbidities, and life expectancy through a Comprehensive Geriatric Assessment. To this aim, where available, a multidisciplinary team of geriatricians, endocrinologists, surgeons, and anesthesiologists is useful for improving risk stratification and prevention (see themes 6 and 7) (groups 1-3).

• To implement pre-hospitalization protocols for patients with known diabetes who need to undergo elective surgery, to maintain a stable metabolic condition (group 1).

• To carry out diabetes screening for patients without a diabetes mellitus diagnosis prior to admission for elective surgery (groups 2 and 3).

• To check and optimize pre- and peri-operative glycemic lowering drugs in persons with a known diagnosis of diabetes mellitus (group 1).

• Define a peri-operative glycemic target range of 100-180 mg/dl. In particular, the CIS and American Diabetes Association suggest targets of < 140 mg/dl for fasting glucose and up to 180 mg/dl during the day [1] (groups 1-3).

• Monitor glucose during the patient's hospital stay: capillary glycaemia should be checked every 4-6 hours for non-critical patients who are unable to feed themselves, while those who regularly eat should be checked preprandially, postprandially, and before they lie down. If the patient is undergoing continuous intravenous infusion, they must be checked every 1-2 hours [2]. The frequency of checks can be reduced (every 4 hours) once glucose levels are stabilized and the infusion rate can be calculated using as algorithm such as the one from Yale University (Goldberg PA, 2005) [2]. Continuous glucose monitoring is not yet recommended during hospitalization [3] (groups 1-3).

• Basal-bolus therapy is the recommended drug regimen for hospitalized diabetic patients, even in hyperglycemic patients without a diagnosis of diabetes (groups 1-3).

2. STRENGTH OF THE RECOMMENDATIONS

The quality of the evidence is moderate. Recommendations are supported

by published evidence and best practice (supported by expert opinion).

3. SUPPORTING EVIDENCE

See appendix.

4. AREAS OF UNCERTAINTY AND FUTURE PERSPECTIVES

In multimorbid, disabled and clinically unstable patients less stringent glycemic targets might be and occasionally are pursued. However, a consensus of opinion about this topic would be desirable.

The safe transition from inpatient to outpatient setting requires a personalized plan. It would be useful to identify patients for whom a comprehensive geriatric assessment at discharge should be preferred to usual care.

APPENDIX

WHAT RECOMMENDATIONS FOR EMERGENCY OR ELECTIVE SURGERY ARE SUGGESTED FOR PATIENTS WITH DIABETES OVER THE AGE OF 75?

Out of the approximately 422 million people with diabetes worldwide (Global Report on Diabetes, WHO 2016), more than 65% are over 65 years old and more than 30% are 75 years or older. Given the direct relationship between age and surgical diseases, the need for surgical procedures among diabetics is likely to increase considerably, especially over 75 [4]. Today, 10% of patients undergoing surgery have a diagnosis of diabetes [5]. Observational studies report that the prevalence of hyperglycemia in patients undergoing surgery, regardless of whether they had a previous diabetes diagnosis, is 32-38% [6], and 80% in cardiac surgery patients [7]. On average, the mortality rate for the surgical population is 50% higher in persons with diabetes compared to those without [8-10].

Studies in the literature report an association between diabetes mellitus and increased risk of post-operative infection [11,12], wound complications [13], cardiovascular events, and venous thromboembolism [14,15]. Diabetes mellitus is also associated with an increased incidence of complications and reoperations [16], post-operative kidney failure [17], and prolonged hospital stay [8,18], leading to increased hospitalization costs.

Studies have compared the outcomes of patients with and without diabetes, based on their pre-and perioperative glycemic values, according to surgery type.

Some analyses [19] have shown that type II patients with moderate glycemic control (150-200 mg/dl) undergoing non-cardiac surgery have comparable mortality and post-operative complications to individuals with well-controlled glycemia (< 150 mg/dl) and lower than those with poor glycemic control (> 200 mg/dl). Stricter blood control, therefore, does not appear to be necessary in this type of patients. In contrast, randomized controlled trials, in the field of cardiac surgery, have shown that glycemic values of 100-140 mg/dl are associated with fewer pre- and post-operative complications [20]. In both surgical and non-surgical cases, 12-38% of patients receiving insulin therapy are hypoglycemic [21]. The development of hypoglycemia, especially in persons over 75, has been associated with longer illness duration and increased in-hospital mortality [22-24].

Studies on pre- and perioperative glycaemia values [25-27] found an increase in the risk of adverse events related to hyperglycemia in non-diabetic patients, but no association among those with diabetes.

HbA1c, which reflects glycemic values over the preceding 90 days, could be used to stratify surgical risk. Most guidelines recommend a value of between 8-9% (68-75 mmol/mol) as a safe target [28]. Among the many studies on pre-operative HbA1c as the only predictive value for post-operative complications, the largest retrospective study was conducted by Adam and colleagues [29] on 40,491 prosthetic knee patients, including 23,924 non-diabetics, 5042 diabetics with HbA1c < 7%, and 2525 diabetics with HbA1c > 7%. Five complications were assessed: 1) revision arthroplasty within one year; 2) infection of the prosthesis within one year; 3) deep venous thrombosis/pulmonary embolism within 90 days; 4) myocardial infarction within one year; 5) all-cause hospitalization within one year. No complications were found to be significantly more frequent in any of the three groups. In particular, total complications were 37% (1877/5042) for those with good glycemic control (HbA1c < 7%) and 34% (857/2525) for those with poor glycemic control. It is known that pre-operative HbA1c values are not in themselves reliable predictors but may be part of a comprehensive patient assessment including age, Body Mass Index, diabetes complications, and comorbidities [30,31].

However, the average age of the population analyzed in the literature is between 60 and 65 years. Older people are often excluded from such studies even though 23% of persons aged 75 and over undergo surgery [32]. In fact, only 1.4% of trials recruit such individuals [33]. Thus, there is limited current knowledge on a population in which diabetes treatment suffers from multimorbidity and polypharmacy, with related risks of adverse events and/or interactions. In addition, patients aged 75+ who undergo surgery have greater post-operative mortality

and an increased risk of complications, both for elective and emergency surgery [34]. Finally, frailty, which is highly prevalent in persons with type II diabetes [35,36], is associated with negative peri-operative outcomes. Identifying frailty could help risk stratification for pre-operative preparation and post-operative management, but evidence is lacking for this specific population.

Insulin is the basis for hyperglycemia treatment. Basal-bolus is the preferred treatment regimen for hospitalized patients, i.e., the use of rapid insulin injections before meals in addition to basal insulin. The RABBIT study showed that, compared to Sliding Scale Insulin (SSI), the basal-bolus method is associated with a reduced incidence of surgical site infection, pneumonia, and respiratory or kidney failure. Despite a better glycemic control, moderate hypoglycemia (< 70 mg/dl) occurred more frequently with the basal bolus regimen. Some non-insulin glucose lowering agents, such as DPP-IV inhibitors, in monotherapy or in combination with basal insulin, could be viable alternatives, especially in older people [2]. Other glucose lowering agents should be avoided in the hospital environment. In particular, the AIFA-AMD-SID Joint Guidelines suggest suspending metformin treatment two days prior to and one day after surgery, replacing it with basal-bolus insulin therapy if necessary.

There are no randomized studies comparing the use of continuous subcutaneous insulin infusion (CSII) with the basal-bolus regimen. The current advice is to suspend CSII at hospital admission and switch to basal-bolus treatment. Intravenous insulin therapy is mainly indicated for the treatment of perioperative hyperglycemia in cardiac surgery, organ transplantation, and cardiogenic shock, as well as during high-dose steroid therapy and parenteral nutrition [2]. Two or three hours before the end of the intravenous insulin therapy, the basal regimen should be administered, using the amount of insulin injected in the last 24 hours as a base for estimating the dose [37].

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This statement is:	Quality of the evidence (in the case of recommendation):
☒ **Recommendation** (supported by published evidence) ☒ **Best practice** (supported by expert opinion)	☐ Low ☒ **Moderate** ☐ High