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Original Article

Influence of age on perioperative major adverse cardiovascular events and mortality risks in elective non-cardiac surgery

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ABSTRACT

Background and aims: Advanced age increases the risk of perioperative cardiovascular complications and may pose reluctance to subject elderly patients to surgery. We examined the impact of high age on perioperative major adverse cardiovascular events (MACE) and mortality in a nationwide cohort of patients undergoing elective surgery.

Methods: All Danish patients aged ≥20 years undergoing non-cardiac, elective surgery in 2005–2011 were identified from nationwide administrative registers. Risks of 30-day MACE (non-fatal ischemic stroke, non-fatal myocardial infarction, or cardiovascular death) and all-cause mortality were analyzed by multivariable logistic regression models (adjusted for comorbidities, revised cardiac risk index, cardiovascular pharmacotherapy, body mass index, and surgery type).

Results: A total of 386,818 procedures on 302,459 patients were included; mean age was 54.8 years (min–max 20–104), and 44% were men. A total of 1297 (0.34%) had perioperative MACE and 1449 (0.37%) died. Advanced age was associated with increased risks of MACE (odds ratio [OR], 1.87; 95% CI, 1.78–1.98 per 10-year high) and mortality (OR, 1.87; 95% CI, 1.78–1.96 per 10-year high). A total of 21,511 procedures were performed on patients >80–90 years old, and 1662 on patients >90 years. The numbers of MACE and crude mortality rates were 331 (1.7%) and 388 (2.0%) among >80–90 years old, and 50 (3.0%) and 67 (4.0%) for those aged >90 years.

Conclusion: The risk of mortality and major adverse cardiovascular events within 30 days after surgery increased with advanced age. However, despite advanced age, the absolute event rates appeared to be relatively modest and around 4% for people aged above 90 years.

1. Introduction

Mobility and morbidity are among the most important factors determining quality of life among elderly, and surgery is often used to treat age related diseases such as osteoarthritis and cancer [1]. Advanced age is, however, also associated with subclinical and overt cardiovascular disease and appears to be an independent risk factor for adverse outcomes in surgery [2,3]. Consequently, high age may pose reluctance to surgery. The American Heart Association concludes in their perioperative guidelines that advanced age is a special risk factor for perioperative myocardial infarction (MI) [4]. These recommendations are based on retrospective cohort studies of selected populations and subgroups of surgeries. Only a few previous studies have investigated the age-associated risks of major adverse cardiovascular events (MACE) and mortality in large and unselected patient materials, and the majority have included limited numbers of very elderly [5,6]. To expand our knowledge on this clinical issue, we investigated the importance of age on MACE and mortality in a contemporary and large-scale sample of patients undergoing elective, non-cardiac surgery in Denmark during a 7-year period.

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2. Methods

The Danish health care system is based on a tax-financed system that covers medical care for all citizens (nearly 6 million people) without copayment. For administrative purposes, the government has kept record on various health-care related variables for many years. By use of a unique social security number (given to all Danish inhabitants at birth or immigration) we cross-linked five of these registries at an individual level to retrieve data on our study cohort. In brief, we obtained information on gender, and dates of birth and deaths from the National Population Registry. From the Danish National Patient Registry we obtained information on admission, operation, and discharge dates and diagnoses of all hospitalizations since 2000. Surgical procedures were classified according to the Nordic Medico-Statistical Committee (NOMESCO) Classification of Surgical Procedures (NCSP) and medical conditions according to the International Classification of Diseases (ICD; the 10th revision has been used since 1994) [7]. These data were generally of high quality since hospital departments were reimbursed based on correct diagnostic and procedural registration [8]. From the National Causes of Deaths Registry we obtained information on causes of deaths (coded according to the ICD-10 system). We obtained information on pharmacotherapy from the Danish Registry of Medicinal Product Statistics, which holds information on all claimed prescriptions from Danish pharmacies since 1995, coded according to the Anatomical Therapeutic Chemical (ATC) classification system [7]. Due to partial reimbursement of medical expenses the registry was very accurate [9]. Pharmacotherapy was defined as claimed prescriptions up to 120 days before surgery [10]. Information on all anesthetic procedures was obtained from the Danish Anesthesia Registry. Available data included information on body mass index (BMI) and whether the surgical procedure was acute or elective.

2.1. Definition of population, comorbidities, cardiovascular pharmacotherapy, and outcomes

We identified all elective neuro, eye, ear–nose–throat, breast, orthopedic, abdominal, plastic, gynecological, endocrine, thoracic (non-cardiac), urological, and vascular surgeries requiring anesthesia performed between January 1 2005 and December 30 2011 (surgery codes are available in E-Table 1). We included those who were ≥20 years old at the time of surgery with only one specialty involved during the same anesthesia (i.e. surgery of more than one organ-type was not included). For individuals who had more than one surgery performed in a 30-day interval, we only included the first surgery in each 30-day period. We reviewed all surgical categories and excluded those that might have been misclassified as elective instead of acute/emergent surgeries in accordance with previous work [11]. We also excluded orthopedic surgeries that were preceded by a diagnosis of trauma to the surgical area, as well as abdominal surgeries preceded by a diagnosis of peptic ulcer or cholecystitis within 7 days prior to surgery. In total, we created 15 surgery subgroups. "Thorax" surgery included pulmonary, mediastinal, and pleural surgeries, "abdominal (bowel)" surgery included esophageal, gastric, duodenal, small intestine, colon, and rectal surgeries, "abdominal (non-bowel)" included all other kinds of abdominal surgeries, "urology" included surgery of the kidneys, ureters, and bladder, "male reproductive" included surgery to the penis, urethra, scrotum, and prostate/seminal glands, "orthopedic minor" included hand, antebrachial, and foot surgeries, "orthopedic major" included all other orthopedic surgeries, "vascular (non-arterial)" included all non-arterial vascular surgeries, and "vascular (arteries)" included the whole arterial system.

Except for diabetes, we identified comorbidities by prior discharge diagnoses in the National Hospitalization Registry at any time up to 5 years prior to the index date. Diabetes was identified by a claimed prescription for glucose-lowering medication (ATC A10) within 120 days prior to surgery [12]. All diagnoses have been validated with good to excellent positive predictive values [13]. Surgery was classified as cancer-related if a cancer diagnosis was identifiable within the year preceding surgery in the same area as the surgery was performed.

We classified patients according to their revised cardiac risk index (RCRI) category based on an accrued risk value between 0 and 6. The RCRI assigned 1 point for each ischemic heart disease (ICD-10 code I20–25), a history of cerebrovascular disease (I60–I69), a history of congestive heart failure (I110, I420, I421, I50), preoperative use of insulin (ATC code A10A), elevated creatinine (originally defined as >2 mg/dL; in the present study defined as a diagnosis of renal disease or need for dialysis [ICD-10 N03, N04, N17–N19, R34, I12, I13, or Z992]), and high-risk surgery (comprising thoracic, intra-abdominal, or suprainguinal aortic surgery). This definition of the RCRI has previously been validated in our registry and was of comparable performance to the original cohort [14].

The main outcome comprised the 30-day risk of MACE (non-fatal acute myocardial infarction [ICD-10 code I21], non-fatal ischemic stroke [ICD-10 code I63 or I64], or cardiovascular mortality [ICD-10 codes I00–I99]).

2.2. Ethics

The study was approved by the Danish Data Protection Agency (ref. no. 2007-58-015 I-suite nr: 02720, GEH-2014-012). In Denmark, retrospective register-based studies do not need ethical approval.

2.3. Statistics

We considered all surgeries as independent observations. Individuals were divided into quintiles of age for the baseline table. We used multivariable logistic regression analyses (including all variables in Table 1) to calculate the odds ratios associated with age as a continuous variable. The linearity assumption of age as a continuous variable was checked using restricted cubic spline functions adjusted for sex, revised cardiac risk index, and surgical groups employing the macro provided by Desquilbet and Mariotti [15] Knots were placed at p10, p25, p50, p75, and p90, and p50 was used as the reference. A two-sided p-value < 0.05 was considered significant for all statistical tests. All statistical analyses were performed in SAS version 9.4 (SAS Institute, Cary, NC).

3. Results

386,818 procedures on 302,459 patients were included with a mean age of 54.8 years (Table 1). Female gender was more prevalent in all age groups, whereas body mass index did not differ markedly across the different age groups. The prevalence of comorbid conditions increased with higher ages and particularly cardiovascular and cancer related diseases were more prevalent in the oldest patients. Use of medications was also higher in groups with advanced age. The RCRI index was also highest in older age groups.

Reproductive, plastic, and ear–nose–throat surgeries were more common in the younger age categories, whereas major orthopedic, cancer related, and vascular surgeries were most often performed in the oldest category.

3.1. The very elderly (>80 years)

In total 21,511 (5.6%) procedures were performed on patients >80–90 years old, and 1662 (0.4%) on patients older than 90 years. Compared with younger patients (<80 years), patients above 80 years more often underwent urological (16.4% vs. 4.9%) and vascular (3.9% vs. 1.3%) surgeries, and less often female reproductive surgery (6.8% vs. 11.9%), non-arterial vessel surgery (2.0% vs. 6.0%), minor orthopedic procedures (3.2% vs. 8.7%), and ear–nose–throat surgery (1.2% vs. 3.3%). Major orthopedic (35.1% vs. 30.4%), abdominal (bowel) (12.5% vs. 13.2%), and abdominal (non-bowel) surgeries (2.3% vs. 1.8%) were not very

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