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Hypertension and intra-operative incidents : a multicentre study of 125,000 surgical procedures in Swiss hospitals

THESE

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Hypertension and intra-operative incidents: a multicentre study of 125 000 surgical procedures in Swiss hospitals

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Rapport de synthèse

Bien que les complications sévères de l'anesthésie soient actuellement rares, des informations contradictoires existent à propos du rôle et de l'importance de l'hypertension artérielle chronique sur la survenue de complications en cours d'anesthésie. En raison de la prévalence élevée de l'hypertension artérielle dans la population et du grand nombre d'anesthésies effectuées, il est important de clarifier cette relation. Le but de l'étude était d'évaluer si les personnes hypertendues étaient à risque accru de présenter des complications lors d'anesthésies à partir de données collectées de routine lors d'anesthésies usuelles réalisées en Suisse.

Nous avons utilisé les données figurant dans le registre ADS (Anesthésie Données Suisse) correspondant à des anesthésies, générales ou locorégionales, réalisées pour chirurgie élective chez des adultes, entre 2000 et 2004 dans 24 hôpitaux suisses. L'attention était portée principalement sur les incidents cardio-vasculaires, mais les autres incidents relevés de routine ont aussi été évalués. La présence d'une hypertension artérielle chronique était définie par la présence d'un traitement antihypertenseur ou par l'anamnèse d'une hypertension artérielle, combinée à la mesure d'une pression artérielle élevée (systolique $\geq$160 mm Hg ou diastolique $\geq$100 mm Hg) lors de l'examen préopératoire de l'anesthésiste. Les incidents relevés en cours d'anesthésie ont été définis a priori et sont enregistrés de routine sur la feuille d'anesthésie et reportés dans une base de données centralisée. En raison de la structure des données, des analyses hiérarchiques ont été effectuées incluant des variables individuelles (niveau 1), liées aux groupes d'interventions chirurgicales (niveau 2) et à l'hôpital (niveau 3).

Parmi les 124 939 interventions, 27 881 (22%) concernaient des patients connus pour une hypertension artérielle chronique. Au moins un incident est survenu dans 16,8% des interventions (95% CI 16,6 -17,0%). Chez 7 549 patients, au moins un incident cardio-vasculaire est survenu, soit dans 6% des anesthésies (95% CI 5.9-6.2%). Le rapport des cotes (odds ratio) moyen ajusté pour les incidents cardio-vasculaires chez les patients hypertendus était de 1.38 (95% CI 1.27-1.49), indiquant une augmentation du risque chez les patients hypertendus. Cependant, l'hypertension n'était pas liée à un risque augmenté de survenue d'un autre incident. Les rapports de cotes ajustés de la survenue d'une complication cardiovasculaire en présence d'une hypertension artérielle variaient selon les hôpitaux entre 0.41 et 2.25.

Ainsi, cette étude confirme la présence d'un risque accru de survenue d'une complication cardiovasculaire chez un patient hypertendu lors d'une anesthésie pour chirurgie élective. Il s'agissait le plus souvent d'une arythmie ou d'une perturbation hémodynamique. Cette augmentation du risque proche de 40% a aussi été trouvée dans une revue systématique avec méta-analyse. L'hétérogénéité des institutions -qui persiste même en tenant compte des ajustements pour le type d'intervention chirurgicale et des variables individuelles (case-mix) - suggère des différences de pratique de l'anesthésie selon l'hôpital.

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Hypertension and intra-operative incidents: a multicentre study of 125 000 surgical procedures in Swiss hospitals*

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Summary

It is debated whether chronic hypertension increases the risk of cardiovascular incidents during anaesthesia. We studied all elective surgical operations performed in adults under general or regional anaesthesia between 2000 and 2004, in 24 hospitals collecting computerised clinical data on all anaesthetics since 1996. The focus was on cardiovascular incidents, though other anaesthesia-related incidents were also evaluated. Among 124 939 interventions, 27 881 (22%) were performed in hypertensive patients. At least one cardiovascular incident occurred in 7549 interventions (6% (95% CI 5.9–6.2%)). The average adjusted odds ratio of cardiovascular risk for chronic hypertension was 1.38 (95% CI 1.27–1.49). However, across hospitals, adjusted odd ratios varied from 0.41 up to 2.25. Hypertension did not increase the risk of other incidents. Hypertensive patients are still at risk of intra-operative cardiovascular incidents, while risk heterogeneity across hospitals, despite taking account of casemix and hospital characteristics, suggests variations in anaesthetic practices.

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Arterial hypertension affects more than one third of the population and is the most frequent comorbidity in patients undergoing surgery [1–3]. The role of hypertension in the occurrence of adverse events in the specific context of peri-operative care is unclear. Some authors have found that neither a diagnosis of hypertension nor elevated blood pressure at admission appear to be a significant risk factor for adverse events following anaesthesia [4–7]. Guidelines issued by the American College of Cardiology and American Heart Association for pre-operative cardiac assessment credit uncontrolled hypertension as being a minor risk, and consider that there is no benefit in delaying surgery in patients with isolated uncontrolled hypertension [8, 9]. Conversely, other investigators have found an increased risk of myocardial infarction, arrhythmias and circulatory instability in patients with poorly controlled hypertension [10–12]. The authors of a recent meta-analysis found that, in hypertensive patients, the odds of peri-operative cardiac complications was 1.3 times higher than in normotensive patients [13]. As a consequence, there is conflicting evidence for whether hypertension represents a risk factor per se for anaesthesia-related adverse events, and particularly cardiovascular ones.

Anaesthesia now being safer, major adverse events are very infrequent and thus of limited value for improving practice. Consequently, routine safety monitoring during the peri-operative period has been extended to a broader range of frequent, but merely undesirable, events [14, 15]. The strong association between those less serious events and major events, and their similar risk factors, supports this approach [16]. Furthermore, minor intra-operative

cardiac events may indeed contribute to serious morbidity over the entire peri-operative period [17, 18].

The purpose of this study was to assess, in a large dataset, routinely collected in patients undergoing anaesthesia, whether patients with chronic arterial hypertension are really at increased risk of intra-operative undesirable events, especially cardiovascular incidents.

Methods

The collection and transmission of the data was specifically authorised by the Federal Data Protection and Information Commissioner within the framework of the Data Protection Law.

The Anaesthesia Databank Switzerland (ADS) was implemented in 1996, as a common electronic dataset on all patients undergoing an operative procedure under regional or general anaesthesia, in a series of voluntary hospitals of various sizes and types located throughout the country. Today, over 40 hospitals participate in ADS. The goal of this project is to foster quality improvement by providing anaesthesia services with feedback on their practice and a benchmark comparison with other hospitals. More detailed information on the ADS project is available online [19]. Every participating hospital collects data for every anaesthetic procedure according to common definitions and format. All information, from entry of the patient into the operating room to departure from the recovery room, is recorded on a standard anaesthetic chart and later entered into a database. Data are then transmitted regularly to the collecting centre, where they are checked for consistency and missing values. All data referring to patients and health professionals are made anonymous before transmission. In addition to the core dataset, hospitals may contribute data to two additional datasets: one relating to management in the operating room and anaesthesia techniques; and one recording anaesthesia-related incidents. Only a subset of hospitals participate to the latter.

The study was conducted on all patients aged 14 years and over undergoing elective surgery between 1 January 2000 and 31 December 2004, in 24 Swiss hospitals. Because of potential underreporting in several hospitals, we excluded endoscopic procedures not requiring incision of the skin or adjacent tissue to have access to the operative site (e.g. gastrointestinal or urinary endoscopy) and obstetric procedures, often performed outside the operating room. Endovascular or laparoscopic operations were included. Incidents occurring in the operating room and until the patient left the recovery room were systematically recorded by members of the anaesthetic team in charge of the patient, by ticking relevant boxes on the anaesthetic sheet according to a pre-established list adapted from Fasting and Gisvold [20]. An uneventful operation was also systematically indicated in a tick-box. An incident was defined as 'a particular event requiring one or more measures taken in order to avoid further deterioration or to treat a situation currently or potentially serious' [20]. Table 1 shows the list and definitions of these incidents. Some events (e.g. arrhythmia) lacked a stringent threshold-based definition. In such cases, the anaesthetist was responsible for reporting; this approach, based on subjective clinical judgment, has been adopted by most voluntary reporting systems [15, 20, 21]. More than one event could be recorded during the surgical intervention. Incidents were aggregated into four clinically relevant groups to provide sufficient events for separate statistical analysis: cardiovascular events; pulmonary events; technical issues; and organisational mishaps. The focus was on cardiovascular events, and the other ancillary endpoints were mainly used to check data quality.

Chronic arterial hypertension was defined as treatment with an antihypertensive drug, or both a history of hypertension (determined by questioning or by a review of all available physician records) and an elevated blood pressure (systolic blood pressure $\geq$ 160 mmHg or diastolic blood pressure $\geq$ 100 mmHg) confirmed by the anaesthetist during the pre-operative visit. The condition was recorded as present or not. No information was available on the severity of the condition, although controlled and uncontrolled hypertension could confer different risks [13]. Comorbidities recorded were: cardiovascular disease (history of myocardial infarction or angina, arrhythmia and any other cardiac disorder, peripheral arterial disease); respiratory disease (tobacco abuse, chronic obstructive pulmonary disease and asthma); renal disease; diabetes mellitus; obesity; and other diseases (including allergy, severe nutritional disorders, coagulation abnormalities, hepatic failure, alcoholism, shock, sepsis, long term corticosteroid treatment, nervous system disease and other significant conditions). The severity of the patient's condition was graded according to the American Society of Anesthesiologists' (ASA) physical status [22].

Surgical interventions were classified according to the 336 SSAR/SGAR (Société Suisse d'Anesthésiologie et de Réanimation/Schweizerische Gesellschaft für Anästhesiologie und Reanimation) categories, a simplified grouping of the International Classification of diseases – version 9, clinical modification (ICD-9-CM) procedures codes (definitions with their matching ICD-9-CM codes available on request from the corresponding author). For statistical purposes, we gathered all surgical interventions into 25 clinically homogeneous surgical groups, according to criteria defined a priori and the level of risk: ear, nose and throat (ENT); ophthalmology; cardiology; urology

Table 1 Definition and frequency of intra-operative adverse events (20 999; 16.8%) in 124 939 anaesthetic interventions. Values are number of events (proportion of interventions) or (proportion of events).

Cardiovascular incidents: n = 7549 (6.0%)		
Hypotension	Decrease of mean arterial blood pressure > 30% of baseline value for > 5 min	3512 (16.7%)
Hypertension	Increase of mean arterial blood pressure > 30% for > 5 min	1275 (6.1%)
Haemodynamic instability	Hypo- and hypertension as defined above	507 (2.4%)
Arrhythmia	New occurrence of arrhythmias (except isolated extrasystolic arrhythmias), including tachycardia and bradycardia	2417 (11.5%)
Myocardial ischaemia	Angina pectoris or change in ECG compatible with myocardial ischaemia	80 (0.4%)
Haemorrhage	Blood loss > 20% (70 ml.kg^{-1})	775 (3.7%)
Related deaths		4 (0%)
Respiratory incidents: n = 935 (0.8%)		
Bronchospasm	Self-explanatory	422 (2.0%)
Hypoxia	Drop of S_pO_2 < 90% for > 5 min or < 80%	362 (1.7%)
Laryngospasm	Self-explanatory	205 (1.0%)
Related deaths		1 (0%)
Technical issues: n = 8348 (6.7%)		
Recovery from anaesthesia	> 10 min after end of surgery and/or administration of antagonistic drug required (except neostigmine)	2671 (12.7%)
Vascular access	Difficulty requiring changing of puncture	2905 (13.8%)
Insertion of tracheal tube	Longer than 40 s, or specific equipment required	1210 (5.8%)
Insufficient sedation	Initial anaesthesia doesn't allow surgery without adding other technique/drugs	1040 (5.0%)
Vomitus or inhalation of gastric contents	During induction or recovery if tracheal tube used, or whole anaesthetic if laryngeal mask airway or face mask used	313 (1.5%)
Hypothermia	Body temperature < 35.5 °C	245 (1.2%)
Allergy	From skin rash to anaphylactic shock (excluding transient skin rash at injection)	150 (0.7%)
Agitation at emergence	Self-explanatory	140 (0.7%)
Dental lesion	Self-explanatory	39 (0.2%)
Related deaths		1 (0%)
Organisational mishaps: n = 3599 (2.9%)		
Waiting time for surgeon	> 5 min (during normal working time)	2679 (12.8%)
Waiting time for anaesthetist	> 5 min (during normal working time)	324 (1.5%)
Equipment failure	Insufficient or no function of equipment (including weak laryngoscope light)	374 (1.8%)
Pre operative drug	Not appropriate	157 (0.8%)
Injury due to surgical position	E.g. corneal lesions, bedsore, plexus lesions	65 (0.3%)
Syringe swap/drug error	Inappropriate drug or dose	64 (0.3%)

(these four divided into two minor/major risk); general; gynaecological; vascular; thoracic; orthopaedic (these five divided into minor/intermediate/major risk); abdominal; neurosurgery; and skin. We conducted sensitivity analysis using different grouping strategies (including no grouping with the 336 SSAR/SGAR categories) to check the consistency of the results.

We also collected: patients' age (divided into 14–25, 26–35, 36–45, 46–55, 56–65, 66–75 and > 75 years) and gender; anaesthetic techniques (general, regional, combined scheduled or combined unscheduled; use of invasive vascular monitoring); other surgical characteristics (duration divided into 1–30 min, 31–60 min, and 1–2, 2–3, 3–4, 4–6, and > 6 h); more than one SSAR/SGAR category performed during the operation); hospital; and calendar year.

Statistical analysis

Bivariate analyses comparing hypertensive and normotensive patients were based on Student's t-test, chi-squared test or Wilcoxon rank-sum test, depending on the type of the independent variable. The ADS data have a hierarchical structure with the individual interventions (level 1) nested in groups of interventions (level 2), which in turn are nested in hospitals (level 3). Therefore, the data are not independent and the intra-cluster correlations between the interventions performed at level 2 and at level 3 have to be accounted for. Multilevel logistic regression analysis was used [23]. Factors at level 1 were related to patients, surgery and anaesthesia characteristics, whereas at levels 2 and 3 only indicator variables were used. The interpretation of models coefficients is similar to that of standard logistic regression, i.e. adjusted log odd ratios (OR), except that they must be interpreted as ORs for within-cluster comparisons and not as population odds as in classical logistic regression analysis (e.g. the OR for chronic hypertension within a specific intervention and in a specific hospital). As the sampling scheme was stratified by hospitals and groups of interventions, these factors were treated as fixed effects. However, because of the large number of intervention groups (particularly when the whole SSAR/SGAR nomenclature was considered) and their very variable sizes, a random effects approach was considered as well, and compared [24].

All covariables were treated as potential confounders and no backward/forward selection was performed.

Two-way level 1 interactions between comorbidities, age, anaesthesia duration and hypertension were retained into the final model based on the conventional level of 5% type 1 error (Wald-tests). Cross-level interactions between chronic hypertension (level 1) and group of interventions (level 2), and chronic hypertension and hospital (level 3), were tested to investigate the heterogeneity of risk between procedures and between hospitals (achieved by including into the model 25 variables HTA × surgical procedure and 24 variables HTA × hospital, and testing the equality of the coefficients to zero). When a significant cross-level interaction was found, the overall mean impact of hypertension was estimated by the weighted mean of each stratum estimates (with weights depending on each stratum size) [25].

All continuous variables were categorised for simpler presentation. Fractional polynomials assessed the functional form of the dose-response relationship and the adequacy of the cut points [26]. Goodness of fit of the model was evaluated using the Hosmer-Lemeshow test and the area under the ROC curve [27]. Given the size of our data sample, focus should rather be on effect size and 95% CI than on p values.

As an additional check of data quality, model adequacy and appropriate adjustment for comorbidities, a model for cardiovascular incidents was estimated, using only patients (with or without hypertension) without other comorbidities. In this population, the effect size of hypertension should, in principle, be comparable to the adjusted estimate obtained from the full sample of data.

All the analyses were performed using SAS version 9.1 and STATA version 9.2 statistical packages.

Results

A total of 124 939 interventions, performed in 24 hospitals, were included in the study. Participating hospitals contributed from 500 to 17 000 operations. About one fifth of interventions (n = 27 881) was carried out in hypertensive patients. Frequencies of adverse events are given Table 1. At least one incident occurred in 16.8% (95% CI 16.6–17.0%) of all interventions and cardiovascular ones in 6% [95% CI 5.9–6.2%], with hypotension the most frequent. While the crude prevalence of hypertension (95% CI) increased almost linearly over the years (19.9% (19.4–20.5%) in 2000, 21% (20.5–21.5%) in 2001, 22.1% (21.6–22.6%) in 2002, 23.5% (23.0–24.1%) in 2003, and 24.1% (23.6–24.6%) in 2004), the rate of all adverse events decreased progressively: cardiovascular from 7.5% (7.1–7.9%) in 2000 to 5.3% (5.0–5.6%) in 2004; respiratory 0.9% (0.81–0.11%) to 0.6% (0.56–0.74%); technical issues 7.1% (6.8–7.5%) to 5.6% (5.3–5.9%); and organisational mishaps 3.3% (3.1–3.6%) to 2.2% (2.0–2.4%).

Table 2 compares hypertensive with normotensive patients. Hypertensive patients were older, more prone to other comorbidities, had higher ASA scores, had longer duration of anaesthesia, and suffered from more intra-operative incidents, except those related to technical issues. They also underwent regional anaesthesia and invasive monitoring more often. The distribution of interventions varied among the two groups as intuitively expected: cardiac, intermediate and major risk vascular operations, major risk urologic, abdominal and orthopaedic interventions were performed more frequently in hypertensive patients; whereas gynaecological, ENT, minor abdominal and orthopaedic surgical interventions were performed less frequently.

Results of the multilevel logistic regression analysis (fixed effects) for cardiovascular events are given in Table 3. After adjusting for the confounding factors at level 1, as well as for the type of procedure (level 2) and hospital (level 3), hypertension was found to be associated with more frequent cardiovascular incidents (overall weighted mean (95% CI) OR 1.38[1] (1.27–1.49)), though the risk was heterogeneous (global test $p < 0.001$) across hospitals, with adjusted OR varying from 0.41 up to 2.25 (Fig. 1). Hypertensive patients showed a significant increased risk in most hospitals, and there was no hospital with a significantly decreased risk. When a random effects model was fitted with level 2 factor, this time using the 336 categories of the SSAR/SGAR nomenclature, the weighted average OR for chronic hypertension was 1.40 (95% CI 1.39–1.52).

The effects of level 1 confounding factors on cardiovascular events are displayed in Table 3. Increasing age and duration of anaesthesia (the first two time categories merged together to avoid empty cells) were strongly associated with the risk of cardiovascular incidents. Multiple procedures during a same operation, ASA physical status and invasive monitoring were weaker risk factors. Among the comorbidities, only cardiovascular disease showed a significant risk. Unexpectedly, diabetes seemed slightly protective. Events risks constantly decreased over calendar years. No interactions between the various comorbidities, or between each comorbidity and hypertension, were found except between cardiovascular disease and hypertension: the OR associated to both conditions was 1.6 instead of 2.0 if the two conditions were additive (see Table 3 footnote). Also,

[1]Corresponding to a mean relative risk of 1.36 according to the formula given in Zhang J & Yu KF. *JAMA* 1998; **280**: 1690–1.

	Hypertension (*n* = 27 881)	No hypertension (*n* = 97 058)	p value
Age; years	68 (13)	48 (18)	< 0.001
Female gender	14 863 (53.3%)	53 946 (55.6%)	< 0.001
ASA score			< 0.001
1	484 (1.7%)	39 455 (40.7%)	
2	15 524 (55.7%)	45 560 (46.9%)	
3	11 110 (39.9%)	11 045 (11.4%)	
≥ 4	784 (2.7%)	998 (1.0%)	
Comorbidity			
None	5040 (18.1%)	31 699 (32.7%)	< 0.001
Cardiovascular	9974 (35.8%)	11 526 (11.9%)	< 0.001
Respiratory	5561 (20.0%)	26 937 (27.2%)	< 0.001
Obesity	6949 (24.9%)	10 930 (11.2%)	< 0.001
Diabetes	4013 (14.4%)	3498 (3.6%)	< 0.001
Renal disease	1488 (5.3%)	1420 (1.5%)	< 0.001
Other	12 429 (44.6%)	42 249 (43.5)	0.002
Type of anaesthesia			< 0.001
General	12 030 (43.2%)	54 719 (56.4%)	
Regional	9374 (33.6%)	25 875 (26.7%)	
Combined (scheduled)	6310 (22.6%)	16 016 (16.5%)	
Combined (unscheduled)	167 (0.6%)	448 (0.5%)	
Duration of anaesthesia; min	117 (75–115 [9–870])	95 (60–140 [9–870])	< 0.001
Invasive monitoring	2178 (8.3%)	3353 (3.7%)	< 0.001
Intra-operative events			
Cardiovascular	3109 (11.2%)	4440 (4.6%)	< 0.001
Respiratory	240 (0.9%)	695 (0.7%)	0.013
Technical issues	1053 (3.8%)	3588 (3.7%)	0.534
Organisational mishaps	1966 (7.1%)	5371 (5.5%)	< 0.001

Table 2 Comparison of normal and hypertensive patients undergoing 124 939 anaesthetic interventions. Values are mean (SD), number (proportion) or median (IQR [range]).

there was no significant interactions between hypertension and age or duration of procedure.

We found the risk of cardiovascular incidents to vary significantly ($p < 0.001$) across surgical procedures (OR 0.46–2.11). Four surgical groups showed significantly lower risk than skin procedures (our reference category): minor cardiac (OR 0.58 (95% CI 0.23–1.51)); major cardiac (0.46 (0.33–0.64)); minor gynaecological (0.74 (0.57–0.95)); and ophthalmological (0.69 (0.51–0.93)). Six groups showed a significantly higher risk: major orthopaedic (1.42 (1.23–1.64)); intermediate thoracic (1.44 (1.10–1.90)); ENT (1.46 (1.22–1.74)); major abdominal (1.48 (1.27–1.73)); major gynaecological (1.74 (1.42–2.14)); and minor thoracic (2.11 (1.46–3.04)). There was no significant interaction with hypertension (global test, p value ≥ 0.145).

We also found large variations of cardiovascular incidents risks between hospitals in non-hypertensive patients, with OR ranging from 0.24 to 2.06 (calculated with reference to the weighted average risk across institutions). These variations reflected systematic differences between hospitals not accounted for by other independent variables. There was no apparent relationship between these ORs and the volume of interventions performed in each hospital (Pearson correlation $\rho = 0.25$; $p = 0.23$).

The discriminative performance of the model was very good, with an area under the ROC curve of 81%. The Hosmer-Lemeshow goodness of fit test was not rejected, with $p = 0.06$ despite the huge sample size.

When the analysis was limited to patients without pre-existing medical conditions except hypertension, the overall weighted mean (95% CI) OR for hypertension was 1.49 (1.21–1.84), i.e. quite similar to the one obtained with the full sample of data where adjustment for the other comorbidities was performed. Furthermore, we found the same heterogeneity of risk between hospitals in this sub-sample.

Regarding the three other endpoints, as expected, we did not find any significant association with chronic hypertension. Respiratory disease, obesity and diabetes were risk factors for respiratory incidents (OR (95% CI) 2.15 (1.84–2.51), 2.35 (1.99–2.78) and 1.42 (1.10–1.82), respectively). Duration of intervention increased this risk, but to a lesser degree than for cardiovascular events (OR 2.2 (1.24–4.04) up to 2 h and 4.5 (2.18–9.62) > 6 h). Regional anaesthesia was strongly protective (OR 0.09 (0.60–0.14)). Unscheduled combined anaesthesia increased the risk of technical issues (OR 29 (24.0–35.3)), as did obesity to a much smaller extent (OR 1.3 (1.22–1.39)). Regional anaesthesia decreased the risk of organisational mishaps (OR 0.83 (0.74–0.92)), whereas duration of anaesthesia increased this risk almost linearly. No comorbidity was significantly associated with increased organisational mishaps.

Table 3 Multilevel logistic regression analysis of cardiovascular incidents in patients undergoing 124 939 anaesthetic interventions. Values are number (95% CI).

Independent variables*	Adjusted OR†	p value
Hypertension	1.38 (1.27–1.49)	< 0.001
Age, years		
26–35	1.51 (1.20–1.89)	< 0.001
36–45	1.87 (1.51–2.31)	< 0.001
46–55	2.41 (1.95–2.97)	< 0.001
56–65	3.60 (2.93–4.43)	< 0.001
66–75	4.84 (3.93–5.96)	< 0.001
> 75	6.31 (5.11–7.81)	< 0.001
Female gender	0.99 (0.93–1.05)	0.772
ASA status		
2	1.23 (1.12–1.34)	< 0.001
3	1.56 (1.39–1.75)	< 0.001
≥ 4	2.07 (1.71–2.50)	< 0.001
Regional anaesthesia	0.79 (0.73–0.85)	< 0.001
Combined scheduled	1.04 (0.96–1.12)	0.292
Combined unscheduled	1.03 (0.76–1.40)	0.858
Invasive monitoring	1.48 (1.34–1.64)	< 0.001
Multiple procedures	1.07 (1.01–1.15)	0.033
Duration of anaesthesia		
31–60 min	4.15 (2.66–6.47)	< 0.001
1–2 h	7.62 (4.92–11.82)	< 0.001
2–3 h	11.51 (7.41–17.90)	< 0.001
3–4 h	15.11 (9.68–23.59)	< 0.001
4–6 h	20.01 (12.77–31.34)	< 0.001
> 6 h	27.48 (17.27–43.73)	< 0.001
Cardiac disease in normotensive subjects	1.50 (1.37–1.64)	< 0.001
Cardiac disease in hypertensive subjects‡	1.62 (1.47–1.79)	< 0.001
Respiratory disease	1.00 (0.94–1.06)	0.945
Obesity	1.07 (1.00–1.15)	0.065
Diabetes	0.89 (0.81–0.98)	0.017
Renal	0.95 (0.83–1.09)	0.473
Other pre-existing disease	1.03 (0.97–1.09)	0.285
Year		
2001	1.11 (1.01–1.22)	0.026
2002	0.84 (0.77–0.92)	< 0.001
2003	0.72 (0.65–0.79)	< 0.001
2004	0.70 (0.64–0.78)	< 0.001

*The reference category was no hypertension, age 14–25 years, male, ASA status 1, general anaesthesia, one procedure, duration ≤30 min, no pre-existing morbidity, year 2000.
†Adjusted for the effect of hospital and type of procedure. Given the relatively low prevalence of cardiac events, the odds ratio (OR) is a very good approximation of the relative risk.
‡Because of the interaction between cardiac disease and hypertension, the OR associated with the two conditions was 1.62 instead of 2.0 if the two conditions were additive.

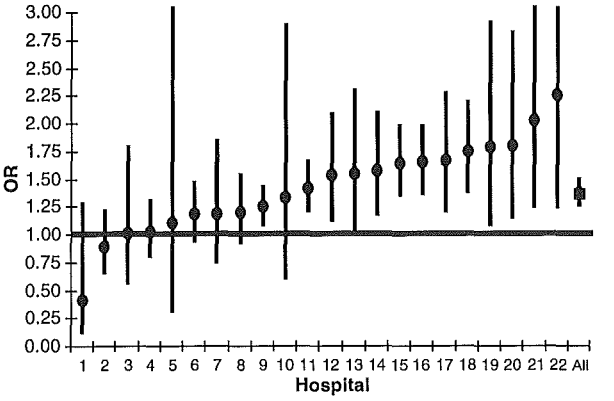

Figure 1 Adjusted odds ratios of cardiovascular events associated with hypertension in patients undergoing 124 939 anaesthetic interventions in 22 hospitals. Two hospitals without any hypertensive patients were excluded. The population averaged value odds ratio of 1.38 is labelled 'all'.

Discussion

Our study clearly shows an independent association of hypertension with an increased risk of developing intra-operative cardiovascular incidents of about 40%. This confirms the findings of the meta-analysis of Howell et al., where similar estimates were obtained from 30 non-experimental studies [13]. Most incidents were arrhythmias and haemodynamic abnormalities. Intra-operative death was extremely rare. Most studies have showed, in fact, that moderate hypertension does not significantly increase the risk of major morbid events [28]. The risk of cardiovascular incidents (and of all incidents as well) decreased regularly over time. It is difficult to say if this reflects a general trend towards safer practices in anaesthesia due to advances in anaesthetic technique or quality improvement driven by the database project.

Beyond statistical significance, one must consider whether an OR of 1.38 for intra-operative incidents, mostly minor, has clinical significance in hypertensive patients undergoing surgery. Although minor, these incidents are not negligible. Intra-operative abnormalities of blood pressure and heart rate have been indeed associated with more severe and even life threatening postoperative adverse outcomes such as stroke, myocardial infarction or ischaemia, prolonged length of stay and hospital death, after cardiac as well as non-cardiac surgery [17, 18, 29]. In addition, an increase in minor incidents might result from substandard processes of care that may, in the long run, be responsible for an increased risk of serious adverse events. The aim of such a monitoring and benchmark quality programme is to help anaesthetic teams to improve their practice. Finally, if one considers the absolute risk increase attributable to hypertension in a patient at a specified baseline risk, the results are clearly relevant [30]. For example, the expected risk (i.e. predicted probability) of cardiovascular events in a 65-year-old patient, ASA 3, experiencing a 5-h operation of mean risk in a hospital of average performance, is estimated in our dataset to be 46% if he has hypertension instead of 32% if he has a normal blood pressure; in this case, hypertension would cause one more incident every

eight patients (95% CI 4–27) [31]. The absolute risk may however be much lower in an individual with another risk profile. Thus, for a patient of 50 years, ASA 3, sustaining a 1-h surgical intervention with an expected control event rate of 3%, hypertension would cause only one more incident every 100 patients (95% CI 40 to ∞).

Whereas the impact of chronic hypertension was independent of the surgical procedure performed, it varied substantially across hospitals. One might argue that these variations reflected differences in casemix, not sufficiently accounted for in our regression model. However, restriction of the analysis to patients with no pre-existing medical condition provided a very similar estimate of the average risk related to hypertension, and a similar heterogeneity of risk among hospitals. Still, data quality could be questioned. The results of the analysis of the other incidents provided sound regression coefficients and risk estimates, supporting good data quality. One may also argue that reporting of incidents may have differed across the hospitals. Nevertheless, the dummy variables used to represent the institutions allowed us to account for this, as well as for other unmeasured hospital characteristics. Consequently, the interaction between the hospital variable and hypertension really do suggest that the risk of events related to hypertension differed across the institutions. Our grouping strategy of operations was based on a priori clinical appraisal, and then meticulously validated by comparing the coefficient estimates obtained in the regression models with other categorisations (SSAR/SGAR nomenclature and other groupings based on translation to ICD-9-CM). In addition, we tested various statistical models with either random or fixed effects. We found consistent results and the same impact of hypertension whatever the model. The large area under the ROC curve illustrated that the most important risk factors for cardiovascular incidents were indeed included into the model.

Variability of outcomes may certainly convey important information regarding the quality of anaesthetic care. Our data, however, do not allow us to identify variations in medical practice. For example, information on anti-hypertensive and anaesthetic drugs was unavailable. Further investigation requiring detailed clinical data is needed before inferring true quality issues during anaesthesia.

To minimise hypertension-related risk during the operative period, some practices are advisable. Beta-blockers, that reduce the incidence of peri-operative cardiac complications, should be continued in treated patients and might be appropriate before surgery for some patients [32]. On the contrary, some authors suggest the withdrawal of specific anti-hypertensive agents (i.e. angiotensin II inhibitors) on the morning of surgery to avoid hypotension after induction [33]. Particular drugs could minimise the hypertensive response to tracheal intubation [34], while hypertensive patients at high risk of haemodynamic disturbance might benefit from pulmonary arterial pressure monitoring [35]. We investigated whether the use of invasive monitoring could explain some risk heterogeneity among hospitals. One may guess that invasive monitoring could detect more incidents, but also prevent some of them. Invasive monitoring was used in < 10% of interventions in all hospitals except one where over 80% of the interventions were performed under such monitoring. Even if the use of invasive monitoring was associated with more frequent incidents, we did not find any correlation with the hospitals' OR of cardiovascular events ($\rho = 0.06$).

There was no clinically significant association between cardiovascular events and any recorded comorbidity except a pre-existing cardiac disease. Surprisingly, diabetic patients showed a slightly lower risk, although the 95% CI only just excluded a value of unity. This may be attributed to the extremely large sample size. At least two previous studies did not find associations between diabetes and intra-operative adverse events or silent postoperative myocardial ischaemia, whereas hypertension was a significant risk [3, 10].

Some ORs related to surgery-specific risk may at first sight appear lower or higher than expected, based on the usual categorisation into low, intermediate and high risk procedures. Cardiovascular surgery, usually considered a high risk procedure, showed no excess risk and major cardiac surgery-related risk was even the lowest. One should note that the ORs for the different procedures were adjusted for the interventions' other characteristics, such as duration and type of anaesthesia, as well as for the patients' characteristics. Therefore, they reflect the residual risk, which is not accounted for by the included factors. Particular attention given to more risky interventions, or use of referral hospitals having highly skilled teams, could explain the lower residual risk of some major elective surgery. Also, cardiac risk stratification is generally linked to 30-day mortality and non-fatal myocardial infarction, and could be different for intra-operative events.

This study bears some strengths and limitations. It benefited from an extremely large number of interventions and events, collected in various hospitals using a standardised protocol, allowing thorough statistical analyses. We assumed that the quality of the routinely collected data was high enough in all hospitals to support the analysis we conducted, especially as there was no bias in adverse events notification. Physicians might be reluctant to report adverse events because of time pressure, fear of punishment, or lack of perceived

benefit [36]. Nevertheless, Fasting & Gisvold, using similar definitions, found similar rates of intra-operative problems (15.7%) [37]. The plausibility of risk factors associated with non-cardiac adverse events, and the OR for hypertension found when the sample was restricted to patients without comorbidity, gave convincing arguments for adequate data quality. The lack of information on the severity of hypertension at admission and on medical practices precludes identification of the causes of the heterogeneous effect of hypertension across hospitals.

In conclusion, chronic hypertension, even isolated, still increases the risk of cardiovascular incidents during anaesthesia by 40%. Even after adjusting for detailed characteristics of casemix, intervention, and hospital, we found important heterogeneity of risk between hospitals suggesting variations in medical practices and room for improvement in the quality of anaesthesia. Although today's guidelines do not consider isolated hypertension as a significant cause of peri-operative cardiovascular morbidity, the anaesthetic management of hypertensive patients must place particular emphasis on maintaining intra-operative haemodynamic stability.

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