REVIEW ARTICLE

Hypertension, hypertensive heart disease and perioperative cardiac risk[†]

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The evidence for an association between hypertensive disease, elevated admission arterial pressure, and perioperative cardiac outcome is reviewed. A systematic review and meta-analysis of 30 observational studies demonstrated an odds ratio for the association between hypertensive disease and perioperative cardiac outcomes of 1.35 (1.17-1.56). This association is statistically but not clinically significant. There is little evidence for an association between admission arterial pressures of less than 180 mm Hg systolic or 110 mm Hg diastolic and perioperative complications. The position is less clear in patients with admission arterial pressures above this level. Such patients are more prone to perioperative ischaemia, arrhythmias, and cardiovascular lability, but there is no clear evidence that deferring anaesthesia and surgery in such patients reduces perioperative risk. We recommend that anaesthesia and surgery should not be cancelled on the grounds of elevated preoperative arterial pressure. The intraoperative arterial pressure should be maintained within 20% of the best estimate of preoperative arterial pressure, especially in patients with markedly elevated preoperative pressures. As a result, attention should be paid to the presence of target organ damage, such as coronary artery disease, and this should be taken into account in preoperative risk evaluation. The anaesthetist should be aware of the potential errors in arterial pressure measurements and the impact of white coat hypertension on them. A number of measurements of arterial pressure, obtained by competent staff (ideally nursing staff), may be required to obtain an estimate of the 'true' preoperative arterial pressure.

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The importance of hypertension

The association between elevated arterial pressure and cardiovascular disease is unequivocally established and well known to doctors and the general public. The risk of cardiovascular events in the general population increases steadily with increases in arterial pressure. The individuals at greatest risk of suffering a cardiovascular event because of hypertension are those with the highest arterial pressures. However, mild to moderate hypertension is more common than severe hypertension, and much of the population burden of disease because of hypertension may be attributed to moderate rather than severe hypertension. This is illustrated in Figure 1, which documents the association between systolic hypertension and deaths as a result of coronary artery disease.⁷⁴ The highest risk of death is seen

in patients with systolic arterial pressures of greater than 180 mm Hg. However, the greatest number of excess deaths (calculated as the difference between the number of deaths that would be expected from coronary artery disease on the basis of the rate in the group with a systolic arterial pressure of less than 110 mm Hg and the number of deaths actually recorded) is seen in the largest group of subjects. That is, those with systolic arterial pressures of between 140 and 149 mm Hg. Hence, medical guidelines for the treatment of hypertension emphasize the treatment of mild to moderate hypertension. The British Hypertension Society Guidelines on the management of hypertension use a threshold of 140/90 mm Hg for the initiation of treatment. ⁶³ This review will

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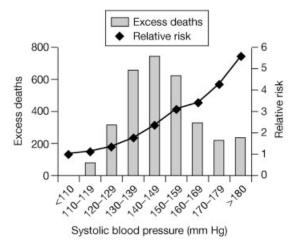


Fig 1 The effect of systolic pressure at entry to MRFIT (Multiple Risk Factor Intervention Trial) on the relative risk of death because of coronary artery disease. The number of excess deaths is calculated relative to the number of deaths because of coronary artery disease that would be expected from the death rate in the baseline group, that is those patients with a systolic arterial pressure of less than 110 mm Hg.⁷⁴

suggest that, while these guidelines are appropriate for the medical management of hypertension, the cut-offs that they use are overly demanding for the management of hypertension in the perioperative setting.

Historical background

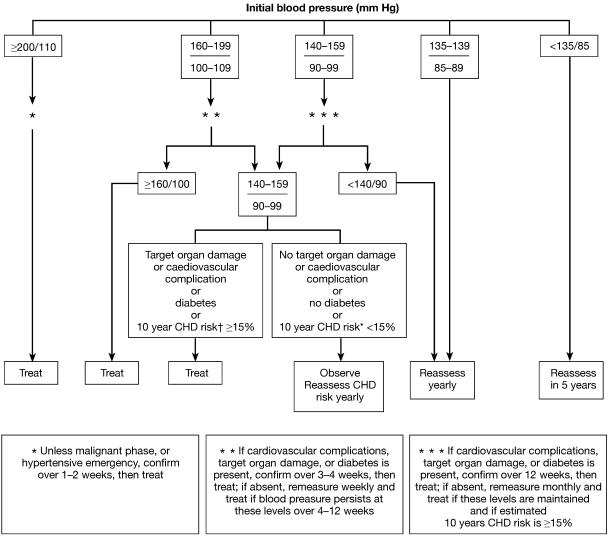
Sprague first identified an association between hypertension and perioperative cardiac risk in 1929. He described a series of 75 hypertensive patients of whom one-third died in the perioperative period; 12 of these had cardiovascular complications.⁷¹

The introduction of antihypertensive drugs led to concerns that patients on such drugs might be at increased risk of perioperative cardiac lability. In 1966, Dingle recommended that patients presenting for anaesthesia and surgery should, if possible, undergo autonomic testing before their operation. This would give some indication of their risk of cardiac lability and whether or not their antihypertensive therapy should be continued.¹⁴ These recommendations were overtaken by the work of Prys-Roberts and colleagues, who published a series of studies on the interaction between hypertension and anaesthesia. The first of these studies examined a small group of 34 patients undergoing anaesthesia and elective surgery. 62 Fifteen of the patients were classified as normotensive, although by current standards all of their control patients would now be considered hypertensive. The remainder of the patients were classified as treated or untreated hypertensives. By current standards, these patients would probably be considered to have severe hypertension as several were reported as having systolic arterial pressures of 220-230 mm Hg. The patients underwent intensive haemodynamic monitoring. The authors reported that the untreated hypertensive patients had a greater decrease in arterial pressure at induction of anaesthesia and that they were more prone to intraoperative myocardial ischaemia. There were no adverse events reported in either the control or hypertensive groups.

On the basis of these findings the authors recommended that, where possible, hypertensive patients should have anaesthesia and surgery deferred to allow their hypertension to be treated. This recommendation led to a major change in anaesthetic practice, and to the modern perception that where possible untreated hypertensives should not be subjected to elective anaesthesia and surgery without first treating their arterial pressure. However, these recommendations should be applied with some caution. The perception of what constitutes hypertension has changed considerably since these studies were undertaken. Arterial pressures that in the early 1970s would have been considered acceptable are today consistent with levels of hypertension where treatment is obligatory. As already stated, all of the control patients in the study by Prys-Roberts and colleagues would now be considered to be hypertensive. The recommendations of Prys-Roberts and colleagues therefore need to be reconsidered in the light of the modern views of hypertension and its management.

The classification of hypertension

It has been indicated above that raised arterial pressure is associated with a continuum of risk, with greatest risk associated with the highest arterial pressures. For the purposes of analysis, discussion and treatment recommendations, it is necessary to grade and classify raised arterial pressure in some way or another. This may be done implicitly by defining treatment thresholds, as in the British Hypertension Society guidelines, or explicitly, by dividing arterial pressure into bands of increasingly severe hypertension, as in the classification of the Sixth Joint National Committee on the Detection, Evaluation and Treatment of High Blood Pressure (JNC VI).35 However, it has been pointed out that the differences between classifications can have major implications for estimating the prevalence of hypertension and the number of people in a population who may require treatment. The World Hypertension Society/ International Society of Hypertension (WHO/ISH) guidelines set lower thresholds than those advocated by either the British Hypertension Society or JNC VI. Acceptance of the WHO/ISH thresholds results in 45% of the population as a whole and 60% of the adult population being classified as hypertensive.⁵¹ It is important to remember the ultimate goals in the treatment of hypertension. These are the reduction of the risk of cardiovascular events for the individual patient and in the population as a whole. Hypertension is only one of a number of risk factors for cardiovascular disease and a number of guidelines, including those issued by the British Hypertension Society, advocate treatment not on the basis of arterial pressure alone but according to the overall estimate of cardiovascular risk (Fig. 2).63



† Assessed with Cardiac Risk Assessor computer program or coronary heart disease risk chart

Fig 2 The British Hypertension Society Guidelines. (CHD = Coronary Heart Disease.) (Reproduced with permission from reference 63.)

Table 1 The classification of hypertension proposed by the Sixth National Committee on the Detection, Evaluation and Treatment of High Blood Pressure³⁵

Category	Systolic arterial pressure (mm Hg)	Diastolic arterial pressure (mm Hg)		
Optimal	<120	<80		
Normal	120-129	80–84		
High Normal Hypertension	130–139	85–89		
Stage 1	140-159	90–99		
Stage 2	160–179	100-109		
Stage 3	≥180	≥110		

For the purposes of this review, the classification of hypertension described in JNC VI will be followed (Table 1).³⁵ This classification is based solely on arterial pressure readings and does not take into account other risk factors, although the importance of taking these into account

when deciding on treatment is highlighted. It defines bands for both systolic and diastolic pressure. Where a patient's systolic and diastolic arterial pressures fall into two different categories, the higher category is selected. It offers a graded classification with six bands of arterial pressure and acknowledges that levels of arterial pressure above optimal pressures of less than 120/80 mm Hg carry some increased risk, while not leading us to classify a large proportion of the population as hypertensive. The anaesthetist is often called upon to take a view on whether or not a given level of arterial pressure is clinically important. The JNC VI classification allows us to identify the place of an individual patient's arterial pressure on a scale of increasing severity. It does, however, have some limitations when applied to the patient presenting for surgery. The most important is that the classification of hypertension is based on the average of two or more readings of arterial pressure taken at two or more visits after initial screening. However, in current British practice, it is uncommon for the anaesthetist to have the benefit of arterial pressure readings taken on a number of recent occasions.

Defining the questions

The perioperative management of hypertensive patients is a complex issue that can be divided into a number of different questions.

- 1. Is having a diagnosis of hypertension of itself associated with increased perioperative risk, regardless of the arterial pressure at the time of admission to hospital for surgery?
- 2. Is elevated arterial pressure at the time of admission for surgery associated with increased perioperative cardiac risk?
- 3. What is the importance, if any, of poorly controlled hypertension in the perioperative setting? Is there any interaction between elevated admission arterial pressure and being diagnosed with hypertensive disease previously such that this increases perioperative risk?
- 4. Does the treatment of elevated admission arterial pressure before surgery reduce perioperative cardiac risk?

For the purposes of this review the term 'hypertensive patient' refers to anyone who has been labelled a hypertensive: that is, someone for whom interventions to lower persistently raised arterial pressure would be appropriate, or someone who is already on treatment for hypertension. Raised arterial pressure will be described as such.

The core of this review will be an examination of the available observational studies that address the first three questions and a discussion of the issues surrounding the interpretation of these studies. Related issues including arterial pressure measurement, white coat hypertension, the use of ambulatory arterial pressure monitoring, and perioperative arterial pressure lability will also be discussed. Recommendations will be offered for the perioperative management of hypertensive patients, although these are based only on observational data. It should be stated at the outset that the authors know of no randomized controlled trial that addresses the final question. The practice of deferring elective surgery to allow poorly controlled arterial pressure to be treated is solely based on the perception that such elevated pressure is associated with increased perioperative risk, and therefore reducing the arterial pressure must be a good thing to do. There is no level one evidence to support this approach.⁷⁶

Hypertensive disease and anaesthesia

This section presents a meta-analysis of observational studies examining the association between hypertension and perioperative cardiac risk in patients undergoing noncardiac surgery. Papers were identified as relevant to the association between hypertension and perioperative cardiovascular outcome if published between 1971 and the end of 2001. The former date was chosen as the lower cutoff year, because this was the year in which the paper 'Studies of anaesthesia in relation to hypertension. I. Cardiovascular responses of treated and untreated patients' was published. ⁶² The MEDLINE database was interrogated using the following combinations of search terms: {anaesthesia OR anesthesia} AND cardiac risk; {anaesthesia OR anesthesia} AND cardiovascular risk; hypertension AND postoperative complication AND adult NOT animal; hypertension AND intraoperative complication AND adult NOT animal; arterial pressure AND intraoperative complication AND adult NOT animal; preoperative risk stratification.

All searches were limited to articles in English. The abstracts of the papers identified were scanned 'on-line' to identify relevant papers. The reference lists of those papers that were identified for inclusion in the meta-analysis were also scanned to identify further relevant studies.

The papers identified from these searches were read in full. Those that included data concerning the association between hypertensive disease and perioperative cardiovascular complications were identified. Reports were included if they examined outcomes considered to be major cardiovascular complications occurring up to 30 days after anaesthesia and surgery. Major cardiovascular complications were considered to be cardiovascular death, myocardial infarction, new or more severe angina, heart failure, life-threatening arrhythmias, and cerebrovascular accident. Several studies examined 'minor' complications such as perioperative bradycardia and tachycardia, and perioperative hypotension and hypertension, and more serious complications. Where it was impossible to separate information on major complications from data on all complications, both major and minor, the study was excluded. Studies that reported the association between hypertension and perioperative myocardial ischaemia detected on Holter monitoring but did not contain data on the association between hypertension and clinically evident events were

For a study to be included, it had to be possible to derive from the report the crude odds ratio for the association between hypertension and perioperative cardiovascular complications, together with the variance of that odds ratio. The ideal would have been to include the adjusted odds ratios in which allowance had been made for the effect of other confounding variables. In most instances, this was not available.

A number of relevant studies were not primarily designed to examine hypertension or other perioperative cardiovascular risk factors, but were studies of diagnostic tests for preoperative cardiovascular assessment or (in one case) of the value of actively warming the patient during surgery. We have included those studies where the report of the study

Table 2 Studies included in the meta-analysis of hypertension and anaesthesia. Note that the odds ratios for the study by Sprung and colleagues⁷² and the studies by Howell and colleagues^{33 34} were derived from paired data

Year	First author	Number of patients	Number of hypertensive patients		Number of normotensive patients		Odds ratio (95% CI)
			With complications	Without complications	With complications	Without complications	(55 % 61)
1978	Steen ⁷⁵	587	17	164	19	387	2.1 (1.1–3.8)
1979	Riles ⁶⁷	683	10	339	6	328	1.6 (0.5-4.5)
1981	Von Knorring ⁸¹	214	10	27	27	150	2.1 (0.9-4.7)
1983	Rao I ⁶⁴	364	9	121	2	232	8.6 (1.8-40.6)
1983	Rao II ⁶⁴	733	3	315	1	414	3.9 (0.4-38.1)
1986	Foster ²¹	1600	66	432	119	983	1.3 (0.9–1.7)
1987	Larsen ⁴¹	2609	18	443	50	2098	1.7 (1.0-3.0)
1989	Eagle ¹⁶	200	18	106	12	64	0.9 (0.4-2.0)
1990	Lette ⁴⁴	60	4	21	5	30	1.1 (0.3–4.8)
1990	Shah ⁶⁹	688	25	325	16	323	1.6 (0.8–3.0)
1992	Lette ⁴³	360	12	171	22	155	0.5 (0.2–1.0)
1992	Pasternack ⁵⁴	385	11	197	8	169	1.2 (0.5–3.0)
1993	Ashton ³	835	7	368	8	452	1.1 (0.4–3.0)
1993	Eichelberger ¹⁸	75	3	53	2	17	0.5 (0.1–3.10)
1994	Poldermans ⁵⁸	131	4	49	11	67	0.5 (0.2–1.7)
1994	Baron ⁵	457	50	168	36	203	1.7 (1.0–2.7)
1995	Gillespie ²⁶	213	17	128	5	63	1.7 (0.5-4.7)
1995	Koutelou ⁴⁰	106	4	51	1	50	3.9 (0.4–36.3)
1995	Ombrellaro ⁵³	266	25	176	13	52	0.6 (0.3–1.3)
1995	Sicari ⁷⁰	136	6	57	3	65	2.3 (0.6–9.5)
1996	Varma ⁷⁸	108	23	76	3	6	0.6 (0.1–2.6)
1996	Kontos ³⁹	87	5	48	9	25	0.3 (0.1–0.9)
1996	Stratmann ⁷⁷	140	7	74	4	55	1.3 (0.4–4.7)
1997	Frank ²²	300	11	199	1	89	4.9 (0.7–38.7)
1998	Badner ⁴	323	13	169	5	136	2.1 (0.7–6.2)
1998	Howell ³⁴	230	54	31	61	84	2.4 (1.3–4.7)
1999	Howell ³³	146	16	19	57	54	1.3 (0.6–2.8)
1999	Heiba ³⁰	101	8	41	9	43	0.9 (0.3–2.6)
2000	Sprung ⁷²	214	86	84	21	23	1.1 (0.6–2.1)
2001	Boersma ⁶	1320	23	560	22	715	1.3 (0.7–2.4)
	Totals	13 671	565	5012	567	7532	1.3 (1.1–1.5)

included relevant data on the association between hypertension and perioperative cardiovascular complications.

A number of studies examining stroke after carotid endarterectomy have been excluded, as it is argued that these studies examined a particular complication in an exceptional population, and the findings from such studies may not generalize to patients undergoing other types of surgery.

The main focus of this meta-analysis was the association between hypertensive disease and perioperative complications, rather than any association between admission arterial pressure and such complications. Consequently, studies that defined hypertension solely in terms of the level of admission arterial pressure were excluded. Studies were included where the definition of hypertension was not given in the report. For example, in the 'Multi-Center Study of General Anesthesia', the anaesthetist was asked to indicate if the patient was hypertensive or not, but the definition of hypertension used is not given.²⁰

A total of 4691 citations were identified from the MEDLINE database. From these, 128 potentially relevant studies were identified from 126 reports. (The full list of 126 citations can be viewed in the version of this review published on the *British Journal of Anaesthesia* website at

http://bja.oupjournals.org/.) For these 128 studies, the full reports were obtained and read in detail. Ninety-eight studies described in 97 reports were excluded from further analysis.

In 80 studies, including the two studies described in a single paper, an effect estimate for the association between hypertension and cardiac complications was not given and could not be derived from the publication. Three studies were excluded because they appeared to include patients who had been examined in another study already included in the meta-analysis. In each case, only one of the pair of papers concerned was included in the meta-analysis. 39 41 58 In six of the excluded studies, hypertension was defined in terms of the arterial pressure alone with no reference to hypertensive disease. In two studies, hypertension was defined as either an elevated admission arterial pressure or a history of treatment with antihypertensive medications and no indication was given of which patients fell into each category. In three of the excluded studies, no distinction was made between major cardiovascular complications such as perioperative myocardial infarction and minor complications such as intraoperative bradycardia. One study was excluded because preoperative coronary artery by-pass grafting and perioperative cardiac complications were

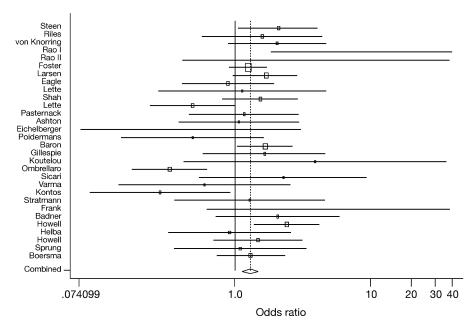


Fig 3 Forrest plot for a meta-analysis of the risk of perioperative cardiovascular complications in hypertensive and normotensive patients. The *x*-axis is on a logarithmic scale. The solid vertical line lies at unity, the dotted vertical line at the combined estimate. For each study, the point estimate of the odds ratio is indicated by the box; the size of the box indicates the size of the study and the weight given to the study. The error bars indicate the 95% confidence intervals for each point estimate.

grouped together as one outcome. Separate information was not given on the association between hypertension and perioperative complications. One study included data on 676 operations in 617 patients. No information was given on which patients underwent more than one procedure. It was felt that using data from this study could lead to an underestimate of the variance of the odds ratio for hypertension and the study was excluded from the meta-analysis. (The full list of excluded studies can be viewed in the electronic version of this paper.)

Initially, it was planned to restrict this review and metaanalysis to patients undergoing general anaesthesia. It rapidly became clear that this was not practical. In those papers containing useful data that also gave information on the type of anaesthesia used a significant proportion of patients received regional or local anaesthesia. Many papers, that did not indicate the type of anaesthesia used, included patients some of whom were likely to have been managed with local regional anaesthesia, for example those undergoing carotid endarterectomy or lower limb revascularization.

Thirty studies were included in the final meta-analysis (Table 2). ³⁻⁶ 16 18 21 22 26 30 33 34 39–41 43 44 53 54 58 64 67 69 70 72 75 77 78 81 These studies were published between 1978 and 2001 and include 12 995 patients. The analysis included two separate studies by Rao and colleagues, both described in the same paper. ⁶⁴ One was a retrospective study of 364 patients anaesthetized between June 1973 and June 1976, and the other a prospective study of 733 patients anaesthetized between July 1977 and June 1982.

A fixed effects meta-analysis of the crude odds ratios from these studies for the association between hypertension and cardiovascular complications was performed using the 'meta' command of Stata v7.0. The Forrest plot of the data is shown in Figure 3. The pooled odds ratio from this analysis was 1.35 (1.17–1.56) P<0.001. However, the test for heterogeneity also achieved statistical significance (Q=44.76, 29 df, P=0.031). (Heterogeneity represents the extent or magnitude of differences in treatment or exposure effects between different studies.)⁵² The source of this heterogeneity was sought through a number of sensitivity analyses grouping the data by year of study (for example 1978–1990 and 1991–2001), and by type of surgery. These analyses yielded little impact on the odds ratio and there remained considerable heterogeneity within the subgroups studied. Thus, the odds ratio of 1.31, while statistically significant, is small and must be interpreted with considerable caution in this meta-analysis of heterogeneous observational studies, with no correction for confounding. In the context of a low perioperative event rate, this small odds ratio probably represents a clinically insignificant association between pre-existing hypertension and perioperative cardiac risk.

Pre-existing hypertension and target organ damage

The association between hypertension and end or target organ damage is well established. Hypertension is inextricably linked to ischaemic heart disease and heart failure, to

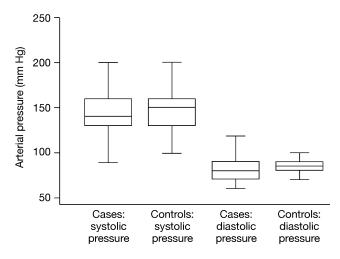


Fig 4 Box and whisker plot of admission systolic and diastolic pressures of cases and controls undergoing elective surgery. The boxes indicate the median values and 25th and 75th centiles. The upper whisker is given by the data point closest to (75th percentile+1.5 (interquartile range)). The lower whisker is given by the data point closest to (25th percentile – 1.5 (interquartile range)). The cases are patients who died of a cardiovascular cause within 30 days of anaesthesia and surgery; the controls are patients matched for type of surgery, age, and sex who did not die of a cardiovascular cause in the perioperative period. There were no significant differences between the admission systolic or diastolic arterial pressures of the cases and the controls. (Reproduced with permission from reference ³⁴.)

cerebrovascular disease and to renal impairment. Both the British Hypertension Society Guidelines and the World Health Organisation-International Society of Hypertension Guidelines for the management of arterial hypertension highlight the importance of co-existing disease and cardiovascular risk factors in setting treatment thresholds. ¹² ⁶³ In both sets of guidelines, the presence of target organ damage and other cardiovascular risk factors lead to lower treatment thresholds for raised arterial pressure.

Similar considerations apply in the perioperative setting. Many reviews have highlighted the associations between the sequelae of hypertension, such as heart failure and ischaemic heart disease, and perioperative complications. 9 15 The meta-analysis of observational studies described above suggested an association between a diagnosis of hypertension and increased perioperative cardiac risk. However, the odds ratio was small and the conclusion must be treated with some circumspection in the light of heterogeneity of the studies examined. This is not to dismiss the role of clinically evident target organ damage in increasing perioperative risk. A recent study by Lee and colleagues identified ischaemic heart disease, heart failure, and renal failure as risk factors for perioperative cardiac complications. 42 In assessing perioperative risk of major cardiovascular complications, pre-existing hypertension per se may be of limited importance, but this does not grant the anaesthetist a licence to ignore the target organ damage caused by hypertension. Such damage may carry significant risk and its importance should be assessed using guidelines such as those referenced above. ⁹ 15

Admission arterial pressure and perioperative cardiac risk

The best-designed study in this area is that of Goldman and Caldera.²⁷ This examined a sub-population of patients who were studied in the production of the Goldman Risk Index. Patients were divided into five groups. These were: normotensive patients, patients treated with diuretics, treated hypertensives whose arterial pressure was controlled, patients who were hypertensive despite treatment, and untreated hypertensives. No significant differences in perioperative cardiac risk were found between the hypertensive patients and the remaining groups. However, although extremely well designed, this study lacked the statistical power to either confirm or refute an association between hypertensive heart disease and perioperative cardiac risk. Other studies, such as those by Cooperman, Eerola, and Steen examined admission arterial pressure as one of a number of variables that may contribute to perioperative cardiac risk. However, these studies either lacked the statistical power to effectively examine hypertension as a risk factor, or gave only limited information on the impact of hypertension in the final report of the study. 13 17 75

None of the studies described above examined admission arterial pressure as a continuous variable. All have taken a specific cut-off for arterial pressure. The only studies of which the authors are aware that have examined arterial pressure as a continuous variable are those by Howell and colleagues. 33 34 The first was a retrospective case controlled study which examined patients who died of a cardiac cause within 30 days of anaesthesia and elective surgery and a matched controlled population who underwent the same operations but who did not die.34 There were no significant differences between admission systolic and diastolic pressures between the cases and the controls (Fig. 4). The second was a similar study of emergency surgery; again there were no significant differences between the arterial pressures of the cases and the controls, although in this case there was a tendency for the survivors to have higher admission arterial pressure than those patients who died.³³ While both of these studies suggest that there is no association between admission arterial pressure and perioperative cardiac risk, they are both limited by the fact that most of the patients studied had Stage 1 or Stage 2 hypertension. Few patients with Stage 3 hypertension were studied.

There is very little evidence on which to base the perioperative management of patients who present for surgery with admission arterial pressures consistent with Stage 3 hypertension. Perhaps the best data come from the original study by Prys-Roberts and colleagues.⁶² In this

study most, if not all, of the hypertensive patients had arterial pressures consistent with Stage 3 hypertension. As already discussed, this study demonstrated increased cardiovascular lability and an increased risk of perioperative myocardial ischaemia in patients with poorly controlled hypertension. It was too small to determine if there was an increased incidence of cardiac events in this population.

The evidence from medical studies suggests that patients with Stage 3 hypertension are at significantly increased risk of target organ damage, whether or not this is clinically evident. For example, Stamler and colleagues, and Liao and colleagues demonstrated a steadily increasing incidence of ECG abnormalities in this population. ^{45 73} There is certainly evidence to support a steadily increasing incidence of postoperative myocardial ischaemia with increasing admission systolic arterial pressure.³¹ Many patients with admission arterial pressures consistent with Stage 3 hypertension will have isolated systolic hypertension. There is evidence from the Framingham population of significantly increased cardiovascular risk in this population. Recent analyses suggest that systolic pressure and pulse pressure are more reliable indicators of cardiovascular risk than diastolic pressure.²⁵ On the basis of these data, we suggest that it is appropriate to defer anaesthesia and surgery where possible in patients with admission arterial pressures consistent with Stage 3 hypertension, especially if there is evidence of target organ damage. However, it must be borne in mind that this recommendation is made on the basis of evidence of risk in medical patients rather than data on perioperative risk. Studies of perioperative risk in patients with Stage 3 hypertension are required.

Isolated systolic hypertension

The steady increase in arterial pressure with age in the Western population is well known. An analysis of data from the Framingham population by Franklin and colleagues has added detail to this picture.²³ They describe a steady increase in systolic arterial pressure starting in childhood and continuing throughout adult life. In contrast, diastolic pressure rises in early adult life and then stabilizes or declines in the fifth and sixth decade of life. There is a steady rise in pulse pressure throughout adult life and the rate of rise increases after the age of 50 yr. It is against this background that the phenomenon of isolated systolic hypertension has been recognized; that is the situation in which the diastolic arterial pressure is normal, but the systolic arterial pressure is elevated. As might be expected, isolated systolic hypertension accounts for the majority of hypertension in patients over 50 yr old. In the NHANES III data, Franklin and colleagues found that 80% of the subjects aged over 50 yr who had hypertension had isolated systolic hypertension.²⁴ As a corollary of this, pulse pressure had been found to be strongly associated with cardiovascular risk.²⁵ The benefits of treating isolated systolic hypertension are now clearly established.²⁹

While the studies of hypertension undertaken by Prys-Roberts and colleagues used the then standard definition of hypertension of a diastolic arterial pressure of greater than 95 mm Hg, it is clear from their publications that many of their patients had severe systolic hypertension. 59-62 Most later studies that have included an examination of the association between admission arterial pressure and perioperative complications have focused on older patients: for example, in the study by Cooperman and colleagues the average age of the patients was 61 yr; in the study by Eerola and colleagues, 69 of the 111 patients studied were over 60 yr old; and in the study of myocardial re-infarction by Steen and colleagues, 361 of the 466 patients studied were aged 60 yr or over. 13 17 75 It is likely that the majority of poorly controlled hypertensives in these studies had isolated systolic hypertension.

A recent study by Aronson and colleagues examined the association between isolated systolic hypertension and cardiovascular complications in patients undergoing cardiac surgery and these data are worth rehearsing here. This was a prospective study of over 2000 patients in 24 centres undergoing elective cardiac surgery. Patients were classified as having normal preoperative arterial pressure, isolated systolic hypertension (systolic arterial pressure greater than 140 mm Hg), diastolic hypertension (diastolic arterial pressure greater than 90 mm Hg) or a combination of these. After adjusting for other risk factors, isolated systolic hypertension was associated with a small but statistically significant increase in the likelihood of perioperative morbidity (odds ratio 1.3, 95% confidence interval 1.1-1.6). The mean systolic arterial pressure of the patients with isolated systolic hypertension is not given, although as the average age of the patients was 65 yr, it is tempting to speculate that it was considerably greater than 140 mm Hg.

It is clear that many of the patients who present for surgery and have arterial pressures consistent with Stage 3 hypertension will be elderly patients with isolated systolic hypertension. There are few if any studies that explicitly examine the impact of isolated systolic hypertension on outcome from non-cardiac surgery and, as with Stage 3 hypertension, work in this area is required. However, the findings of the study by Aronson and colleagues and the work of Franklin and colleagues on the Framingham population do little to reassure the anaesthetist.

White coat hypertension

So-called white coat hypertension is directly relevant to anaesthetic practice. It is formally defined as a persistently elevated clinic arterial pressure in combination with a normal ambulatory arterial pressure. So Various different arterial pressure thresholds have been used to define white coat hypertension in different studies, leading to conflicting data as to the prognosis of this condition. Recently, criteria have been agreed and are now widely accepted. These define white coat hypertension as an office arterial pressure

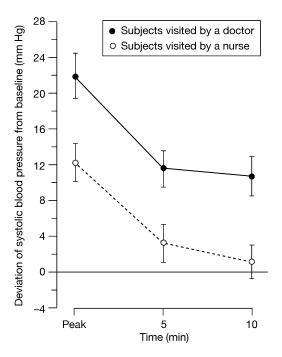


Fig 5 Comparison of systolic arterial pressure changes in 30 subjects (10 normotensive and 20 hypertensive) when subjects were visited by doctor (solid line) and a nurse (dashed line) and three arterial pressure readings taken with a sphygmomanometer at the 2nd, 5th, and 8th minute of the visit. All arterial pressures values shown in the graph were obtained from a transducer attached to an intra-arterial cannula. Values were recorded by a mini-tape recorder and were not visible to the visiting doctor or nurse. Baseline arterial pressures were obtained from the intra-arterial cannula readings taken 4 min before the visit of the doctor or nurse. The y-axis shows the peak deviation from this baseline arterial pressure and the arterial pressures 5 and 10 min later. Values shown are mean (SEM).⁴⁷ (Modified with permission from reference ⁴⁷.)

of 140/90 mm Hg or greater in the presence of an average daytime reading of less than 135/85 mm Hg. 50 56 Pickering and colleagues highlight the difficulties in comparing different studies in this area, but suggest that the majority of the data indicate a benign prognosis for white coat hypertension. 56 Kaplan identifies four prospective studies of prognosis of hypertension that support this view. ³⁶ ³⁸ ⁵⁵ ⁶⁵ ⁸⁰ The largest of these, by Verdecchia and colleagues, followed up 1522 hypertensive subjects for 10 yr. Using a conservative definition of white coat hypertension, based on an ambulatory arterial pressure of less than 130/90 mm Hg, this study found the rate of cardiovascular events in white coat hypertension (0.67/100 patient yr) to be little different to that seen in normotensives.80 It should be noted that when more liberal definitions of white coat hypertension, with a higher ambulatory arterial pressure, were used, the cardiovascular event rate in patients with white coat hypertension was close to that of 'true' hypertensives. These data suggest that patients who present for elective surgery with admission arterial pressures consistent with Stage 3 hypertension that then settle to levels consistent with normotension may be at less risk of cardiovascular complications than patients with sustained

hypertension. However, extrapolating from data derived from a long-term study conducted in the medical setting to draw conclusions about patients undergoing surgery is a leap, and any conclusions drawn have to be treated with some caution.

The various guidelines on the management of hypertension all indicate that the arterial pressure should be measured on a number of occasions over a period of weeks before the diagnosis of hypertension is confirmed. It is rare for the anaesthetist to have this luxury and often a decision has to be made on perioperative management on the basis of two or three readings taken over a period of hours.

Both doctors and nurses may produce an initial elevation in arterial pressure when they visit a patient, but the effect is greater for doctors than for nurses. This is impressively illustrated by data from Mancia and colleagues. They studied 30 subjects who underwent a 24-h intra-arterial recording after 5-7 days in hospital. During the intra-arterial recording period the arterial pressure was additionally measured at different times using a sphygmomanometer by a male doctor and a female nurse, half of the subjects being randomized to see the doctor first, and the other half the nurse. When the doctor took the first reading, the arterial pressure rose by an average of 22/14 mm Hg. The rises when the first arterial pressure was taken by a nurse were only half as great. The arterial pressure usually returned to near baseline after 10 min when the reading was taken by a nurse, but this was not the case when the pressure was taken by a doctor (Fig. 5).⁴⁷ It is clear from their data that, in many surgical patients, the admission arterial pressure will not equate to the patient's usual arterial pressure. If a member of the medical staff finds the patient's arterial pressure to be elevated, this should be confirmed by a nurse with appropriate training.

Cardiovascular lability

Patients diagnosed as 'hypertensive' have a reputation for displaying increased cardiovascular lability during anaesthesia. There is certainly a pathophysiological basis for such behaviour. Established hypertension is associated with an increased systemic vascular resistance.³⁶ The systemic vasodilatation associated with anaesthesia might well be expected to have profound effects on arterial pressure in such patients. Prys-Roberts and colleagues, and Goldman and Caldera both demonstrated that induction of anaesthesia is associated with a decrease in arterial pressure to a similar nadir in both hypertensive and normotensive patients.^{27 62} However, because hypertensive patients in these studies generally had a higher pre-induction arterial pressure, absolute decrease in arterial pressure in these patients was greater. For many anaesthetists, however, cardiovascular lability implies something more than the decrease in arterial pressure seen at induction of anaesthesia. It suggests swings in arterial pressure over a wide range of values, graphically described by Longnecker as 'Alpine Anesthesia'. 46 Prys-

Roberts and colleagues established that poorly controlled hypertensive patients have a more vigorous cardiovascular response to laryngoscopy and intubation than do normotensives or well controlled hypertensives. 61 Studies by Charleson and colleagues documented swings in arterial pressure in hypertensive and diabetic patients. 78 However, their work makes no comparison between hypertensive and normotensive patients in respect to their cardiovascular behaviour, and neither confirms nor refutes the suggestion that hypertensives are particularly prone to cardiovascular instability. Chung and colleagues examined the association between pre-existing medical conditions and adverse events in 17 638 patients undergoing day-case surgery. 11 They identified an association between pre-existing hypertension and intraoperative cardiovascular events. No major complications, such as death or perioperative infarction, are reported and the majority of these cardiovascular events were episodes of hypertension, although there were also instances of hypotension and arrhythmia. In the large 'Multicenter Study of General Anesthesia', it was noted that hypertensive patients were more likely to require interventions for perioperative hypertension. 19 However, the definition of hypertension used in this study was not given in the report. Taken together, the weight of the evidence is that patients with hypertension may be expected to suffer a greater decrease in arterial pressure at induction of anaesthesia than normotensive patients, although the arterial pressure probably decreases to a similar nadir in both patient groups. The work of Prys-Roberts and colleagues supports a more vigorous response to noxious stimuli in these patients. The findings of Chung and colleagues indicate that patients with pre-existing hypertension frequently have high arterial pressures during the intraoperative period.¹¹

The clinical impact of wide variations in arterial pressure is difficult to quantify, not least because most anaesthetists would not be prepared to leave large changes in arterial pressure untreated for more than a short period of time. Charleson and colleagues reported that, within a high-risk group of hypertensive patients and diabetic patients undergoing elective non-cardiac surgery, those with more than 1 h of a decrease in mean arterial pressure of greater than/equal to 20 mm Hg and those with less than 1 h of a decrease in arterial pressure of greater than/equal to 20 mm Hg and more than 15 min of an increase in arterial pressure of greater than/equal to 20 mm Hg were at greatest risk of complications. In so far as we can tell, the use of vasoactive drugs was allowed in the perioperative period. One has to ask if, in the patients who had wide excursions of arterial pressure, a decision was made not to treat these changes in arterial pressure or if the changes in arterial pressure were refractory to treatment because of ongoing perioperative cardiovascular complications. The association between intraoperative myocardial ischaemia and haemodynamic changes is certainly not clear-cut. In a study of 100 patients who either had, or were at risk for, coronary artery disease, intraoperative ischaemic episodes were preceded by acute increases in arterial pressure in only 15% of episodes and by acute decreases in only 8% of episodes. ⁴⁸ A recent paper by Reich and colleagues has described an association between intraoperative hypertension and tachycardia and adverse outcome in protracted surgery. ⁶⁶ It was by no means clear, however, that this was a causal association.

Perioperative management of patients with hypertension or raised arterial pressure

The meta-analysis presented above suggests association between a diagnosis of hypertension and increased perioperative cardiac risk. However, the odds ratio for the effect of hypertension was small and the conclusion must be treated with some circumspection in the light of heterogeneity of the studies examined. There is evidence from many studies that conditions that may represent target organ damage as a result of hypertension contribute to perioperative cardiac risk. A study by Lee and colleagues identified ischaemic heart disease, heart failure, and renal failure as risk factors for perioperative cardiac complications. It would seem sensible to suggest that anaesthetists should pay more heed to the presence of significant target organ damage than to a diagnosis of hypertension *per se*.

With regard to the management of surgical patients with elevated admission arterial pressure, there are few substantive guidelines over which patients should be cancelled to allow treatment before surgery or the duration of such treatment before proceeding with surgery. The American Heart Association/American College of Cardiology (ACC/AHA) guidelines comment that hypertension (Stages 1 and 2) is not an independent risk factor for perioperative cardiovascular complications. However, they suggest that Stage 3 hypertension (SAP ≥ 180 mm Hg and/or DAP ≥ 110 mm Hg) should be controlled before surgery. To quote the guidelines:

'In many instances establishment of an effective treatment regimen can be achieved over several days to weeks of preoperative outpatient management. If surgery is more urgent, rapid acting agents can be administered to allow effective control in a matter of minutes or hours. Betablockers appear to be particularly attractive agents. Continuation of preoperative antihypertensive treatment through the perioperative period is critical.'

The observational data presented in this review support the recommendations for Stages 1 and 2 hypertension. The AHA/ACC recommendations for Stage 3 hypertension are not supported by substantial data relating exclusively to patients with arterial pressures greater than 180/110 mm Hg. The best perioperative management of these patients remains unclear. The options available to the anaesthetist are: to ignore the elevated arterial pressure and to continue with anaesthesia and surgery; to institute acute treatment to control the arterial pressure; or to defer surgery for a period of weeks to allow the arterial pressure to be controlled.

High arterial pressures are associated with high levels of after load and cardiac work. This may predispose to myocardial ischaemia and infarction, especially in the presence of coronary artery disease and left ventricular hypertrophy, and therefore simply ignoring markedly elevated arterial pressure may not be appropriate. However, there is evidence that very rapid control of arterial pressure with drugs such as sublingual nifedipine is associated with increased morbidity and mortality. Taken together, these concerns pose the dilemma that markedly raised arterial pressures and wide excursions of arterial pressure should be avoided in the perioperative period, but that dramatic acute reductions in arterial pressure may also be fraught with risk.

Observational data lend weight to these concerns. The work of Charleson and colleagues suggests that excursions in mean arterial pressure of greater than 20% in patients with hypertension and or diabetes are associated with perioperative complications.8 The work of Gould and colleagues indicates that marked perioperative reductions in arterial pressure may be associated with reduced splanchnic blood flow even in the 'well filled' patient.²⁸ The best course of action for the anaesthetist would seem to be to defer surgery to allow the arterial pressure to be treated. However, there are no trial data to suggest that this strategy reduces perioperative risk and this advice takes no account of the many issues and problems associated with cancelling an operation within 24 h of surgery. Also, if surgery is deferred to allow the arterial pressure to be treated, it is unclear for how long treatment should be given before the patient returns to have his or her operation.

Weksler and colleagues reported recently the results of a clinical trial in which patients were brought to a waiting room in the operating theatre suite, sedated with midazolam, and had their diastolic pressures measured whilst awaiting surgery. 82 989 patients whose diastolic arterial pressure was between 110 and 130 mm Hg immediately before surgery were entered into the trial. 589 patients were randomized to receive nifedipine 10 mg administered intranasally, while 400 patients were randomized to have their surgery postponed. Those patients in whom surgery was deferred remained in hospital until the diastolic arterial pressure was below 110 mm Hg for at least 3 consecutive days. The frequency of perioperative hypotension and hypertension was similar in the two groups, as was the incidence of tachyarrhythmias and bradyarrhythmias. There were no neurological or cardiovascular complications in either group. This study has a number of weaknesses. It was not blinded, it ran over a 9-yr period, during which many other aspects of patient management could have changed, and systolic hypertension was not studied. However, it offers no support for deferring anaesthesia and surgery to allow the arterial pressure to be treated.

We suggest that, if the patient is considered fit for surgery in other respects, their operation should not be deferred simply on account of an elevated admission arterial pressure. If the arterial pressure is consistently elevated to levels of 180 mm Hg systolic or greater or 110 mm Hg diastolic or greater, surgery may proceed, but care should be taken to ensure perioperative cardiovascular stability. Invasive arterial pressure monitoring is indicated for major procedures, and the arterial pressure should be actively managed to prevent excursions of the mean arterial pressure of greater than 20% from baseline. Monitoring should continue into the postoperative period until it is clear that the patient is cardiovascularly stable. It may be appropriate to manage the patient in a high dependency area in the immediate postoperative period. In those patients in whom there is no contraindication, perioperative betaadrenergic block may be of value. These drugs are known to reduce perioperative myocardial ischaemia and cardiovascular complications in high-risk patients. 49 57 They carry the additional merit of not producing marked arterial pressure reductions in normotensive subjects. It should be pointed out that Boersma and colleagues have produced observational data that support the widespread use of perioperative beta-adrenergic blockade, but that the available data from randomized controlled trials only provide clear support for their use in high-risk patients with demonstrable new wall motion abnormalities on dobutamine stress echocardiography. 6 32 Clinical trial data to support the use of perioperative beta-adrenergic block in other patients with cardiac disease are awaited. There may be a place for other sympatholytic therapies such as alpha-2 agonists or thoracic epidural block. The pharmacology and use of the alpha-2 agonists has been reviewed by Khan and colleagues.³⁷ A meta-analysis by Rogers and colleagues suggested that neuroaxial block does offer protection from perioperative myocardial injury.⁶⁸ The validity of this finding has been challenged and the current position remains unclear.¹ Although Weksler and colleagues reported no problems with intranasal nifedipine administered to 589 patients immediately before surgery, we are unable to recommend its use because of the concerns expressed by Varon and colleagues. 79 82

In making clinical judgements about perioperative management, white coat hypertension is an ever-present problem. If the preoperative arterial pressure is giving cause for concern, several further readings should be obtained by someone who is competent to do so. It seems indefensible to defer planned surgery on the basis of a single arterial pressure reading. In view of the vigorous alerting reaction that can be produced by a visit from a doctor, readings obtained by an experienced nurse may be invaluable. If at all possible, the patient's family doctor should be contacted and enquiry made about arterial pressure readings obtained in the family practitioner's office. It must be a source of irritation for the patient and family doctor for surgery to be deferred and the patient be sent back for treatment of their arterial pressure when the they have been on carefully monitored treatment for months or years and the arterial pressure is known to be well controlled.

Addendum

During the preparation of this review, there has been published the Seventh Report of the Joint National Committee on prevention, detection, evaluation and treatment of high arterial pressure (2003). This recognizes that the risk of cardiovascular disease begins at a pressure of 115/75 mm Hg and doubles with each increment of 20/10 mm Hg. Individuals with a systolic arterial pressure of 120– 139 mm Hg or diastolic arterial pressure of 80–89 mm Hg should be considered as pre-hypertensive. The JNC VII classifies arterial pressure in adults as: normal: systolic arterial pressure greater than 120 mm Hg and diastolic arterial pressure less than 80 mm Hg; pre-hypertension: systolic arterial pressure 120-139 mm Hg or diastolic arterial pressure 80-89 mm Hg; Stage I hypertension: systolic arterial pressure 140-159 mm Hg or diastolic arterial pressure 90-99 mm Hg; Stage II hypertension: systolic arterial pressure greater than 160 mm Hg or diastolic arterial pressure greater than 100 mm Hg.

As in previous publications from the JNC, there are no recommendations or guidelines for the perioperative care of the hypertensive patient.¹⁰

Longer version of this paper

A longer version of this paper can be found in *British Journal of Anaesthesia* on-line as supplementary data.

References

- I Which anaesthetic technique? Bandolier 2001; 86: 5
- 2 Aronson S, Boisvert D, Lapp W. Isolated systolic hypertension is associated with adverse outcomes from coronary artery bypass grafting surgery. Anesth Analg 2002; 94: 1079–84
- 3 Ashton CM, Petersen NJ, Wray NP, et al. The incidence of perioperative myocardial infarction in men undergoing noncardiac surgery. Ann Intern Med 1993; 118: 504–10
- 4 Badner NH, Knill RL, Brown JE, Novick TV, Gelb AW. Myocardial infarction after noncardiac surgery. *Anesthesiology* 1998; **88**: 572–8
- 5 Baron JF, Mundler O, Bertrand M, et al. Dipyridamole-thallium scintigraphy and gated radionuclide angiography to assess cardiac risk before abdominal aortic surgery. N Engl J Med 1994; 330: 663–9
- 6 Boersma E, Poldermans D, Bax JJ, et al. Predictors of cardiac events after major vascular surgery: role of clinical characteristics, dobutamine echocardiography, and betablocker therapy. JAMA 2001; 285: 1865–73
- 7 Charlson ME, MacKenzie CR, Gold JP, et al. The preoperative and intraoperative hemodynamic predictors of postoperative myocardial infarction or ischemia in patients undergoing noncardiac surgery. Ann Surg 1989; 210: 637–48
- 8 Charlson ME, MacKenzie CR, Gold JP, Ales KL, Topkins M, Shires GT. Intraoperative blood pressure. What patterns identify patients at risk for postoperative complications? *Ann Surg* 1990; 212: 567–80
- 9 Chassot PG, Delabays A, Spahn DR. Preoperative evaluation of patients with, or at risk of, coronary artery disease undergoing non-cardiac surgery. Br J Anaesth 2002; 89: 747–59

- 10 Chobanian AV, Bakris GL, Black HR, et al. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. JAMA 2003; 289: 2560–72
- 11 Chung F, Mezei G, Tong D. Pre-existing medical conditions as predictors of adverse events in day-case surgery. Br J Anaesth 1999; 83: 262–70
- 12 Committee of World Health Organisation-International Society of Hypertension. 1999 World Health Organization-International Society of Hypertension (WHO-ISH). Guidelines for the Management of Hypertension. J Hypertens 1999; 17: 151–83
- 13 Cooperman M, Pflug B, Martin EW, jr, Evans WE. Cardiovascular risk factors in patients with peripheral vascular disease. Surgery 1978: 84: 505–9
- 14 Dingle HR. Antihypertensive drugs and anaesthesia. Anaesthesia 1966; 21: 151–72
- 15 Eagle KA, Berger PB, Calkins H, et al. ACC/AHA guideline update for perioperative cardiovascular evaluation for noncardiac surgery. A report of the American College of Cardiology/ American Heart Association Task Force on Practice Guidelines (Committee to Update the 1996 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery). 2002. American College of Cardiology Web site. Available at http./ www.acc.org/clinical/guidelines/perio/driIndex.htm
- 16 Eagle KA, Coley CM, Newell JB, et al. Combining clinical and thallium data optimizes preoperative assessment of cardiac risk before major vascular surgery. Ann Intern Med 1989; 110: 859–66
- 17 Eerola M, Eerola R, Kaukinen S, Kaukinen L. Risk factors in surgical patients with verified preoperative myocardial infarction. Acta Anesthesiol Scand 1980; 24: 219–23
- 18 Eichelberger JP, Schwarz KQ, Black ER, Green RM, Ouriel K. Predictive value of dobutamine echocardiography just before noncardiac vascular surgery. Am J Cardiol 1993; 72: 602–7
- 19 Forrest JB, Rehder K, Cahalan MK, Goldsmith CH. Multicenter study of general anesthesia. III. Predictors of severe perioperative adverse outcomes. Anesthesiology 1992; 76: 3–15
- 20 Forrest JB, Rehder K, Goldsmith CH, et al. Multicenter study of general anesthesia. I. Design and patient demography. Anesthesiology 1990; 72: 252–61
- 21 Foster ED, Davis KB, Carpenter JA, Abele S, Fray D. Risk of noncardiac operation in patients with defined coronary disease: the Coronary Artery Surgery Study (CASS) registry experience. Ann Thorac Surg 1986; 41: 42–50
- 22 Frank SM, Fleisher LA, Breslow MJ, et al. Perioperative maintenance of normothermia reduces the incidence of morbid cardiac events. A randomized clinical trial. JAMA 1997; 277: 1127–34
- 23 Franklin SS, Gustin W 4th, Wong ND, et al. Hemodynamic patterns of age-related changes in blood pressure. The Framingham Heart Study. Circulation 1997; 96: 308–15
- 24 Franklin SS, Jacobs MJ, Wong ND, L'Italien GJ, Lapuerta P. Predominance of isolated systolic hypertension among middle-aged and elderly US hypertensives: analysis based on National Health and Nutrition Examination Survey (NHANES) III. Hypertension 2001; 37: 869–74
- 25 Franklin SS, Khan SA, Wong ND, Larson MG, Levy D. Is pulse pressure useful in predicting risk for coronary heart disease? The Framingham heart study. *Circulation* 1999; 100: 354–60
- 26 Gillespie DL, LaMorte WW, Josephs LG, Schneider T, Floch NR, Menzoian JO. Characteristics of patients at risk for perioperative myocardial infarction after infrainguinal bypass surgery: an exploratory study. Ann Vasc Surg 1995; 9: 155–62
- 27 Goldman L, Caldera DL. Risks of general anesthesia and elective

- operation in the hypertensive patient. Anesthesiology 1979; 50: 285–92
- 28 Gould TH, Grace K, Thorne G, Thomas M. Effect of thoracic epidural anaesthesia on colonic blood flow. Br J Anaesth 2002; 89: 446–51
- 29 Group for Collaborative Research: Systolic Hypertension in the Elderly Program. Prevention of stroke by antihypertensive drug treatment in older persons with isolated systolic hypertension. Final results of the Systolic Hypertension in the Elderly Program (SHEP). JAMA 1991; 265: 3255–64
- 30 Heiba SI, Jacobson AF, Shattuc S, Ferreira MJ, Sharma PN, Cerqueira MD. The additive values of left ventricular function and extent of myocardium at risk to dipyridamole perfusion imaging for optimal risk stratification prior to vascular surgery. Nuclear Med Commun 1999; 20: 887–94
- 31 Howell SJ, Hemming AE, Allman KG, Glover L, Sear JW, Foex P. Predictors of postoperative myocardial ischaemia. The role of intercurrent arterial hypertension and other cardiovascular risk factors. Anaesthesia 1997; 52: 107–11
- 32 Howell SJ, Sear JW, Foex P. Peri-operative beta-blockade: a useful treatment that should be greeted with cautious enthusiasm. Br J Anaesth 2001; 86: 161–4
- 33 Howell SJ, Sear JW, Sear YM, Yeates D, Goldacre M, Foex P. Risk factors for cardiovascular death within 30 days after anaesthesia and urgent or emergency surgery: a nested casecontrol study. Br J Anaesth 1999; 82: 679–84
- 34 Howell SJ, Sear YM, Yeates D, Goldacre M, Sear JW, Foex P. Risk factors for cardiovascular death after elective surgery under general anaesthesia. Br J Anaesth 1998; 80: 14–9
- 35 Joint National Committee on prevention detection, evaluation, and treatment of high blood pressure. The sixth report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure. Arch Intern Med 1997; 157: 2413–46
- 36 Kaplan NM. Clinical Hypertension, 8th edn. Philadelphia: Lippincott Williams and Wilkins, 2002; 35–36, 92–96
- 37 Khan ZP, Ferguson CN, Jones RM. Alpha-2 and imidazoline receptor agonists. Their pharmacology and therapeutic role. Anaesthesia 1999; 54: 146–65
- 38 Khattar RS, Senior R, Lahiri A. Cardiovascular outcome in white-coat versus sustained mild hypertension: a 10-year follow-up study. Circulation 1998; 98: 1892–7
- 39 Kontos MC, Brath LK, Akosah KO, Mohanty PK. Cardiac complications in noncardiac surgery: relative value of resting two-dimensional echocardiography and dipyridamole thallium imaging. Am Heart J 1996; 132: 559–66
- 40 Koutelou MG, Asimacopoulos PJ, Mahmarian JJ, Kimball KT, Verani MS. Preoperative risk stratification by adenosine thallium 201 single-photon emission computed tomography in patients undergoing vascular surgery. J Nuclear Cardiol 1995; 2: 389–94
- 41 Larsen SF, Olesen KH, Jacobsen E, et al. Prediction of cardiac risk in non-cardiac surgery. Eur Heart J 1987; 8: 179–85
- 42 Lee TH, Marcantonio ER, Mangione CM, et al. Derivation and prospective validation of a simple index for prediction of cardiac risk of major noncardiac surgery. Circulation 1999; 100: 1043–9
- 43 Lette J, Waters D, Bernier H, et al. Preoperative and long-term cardiac risk assessment. Predictive value of 23 clinical descriptors, 7 multivariate scoring systems, and quantitative dipyridamole imaging in 360 patients. Ann Surg 1992; 216: 192–204
- 44 Lette J, Waters D, Lassonde J, et al. Postoperative myocardial infarction and cardiac death. Predictive value of dipyridamolethallium imaging and five clinical scoring systems based on multifactorial analysis. Ann Surg 1990; 211: 84–90
- 45 Liao YL, Liu KA, Dyer A, et al. Major and minor electro-

- cardiographic abnormalities and risk of death from coronary heart disease, cardiovascular diseases and all causes in men and women. *J Am Coll Cardiol* 1988; 12: 1494–500
- 46 Longnecker DE. Alpine anesthesia: can pretreatment with clonidine decrease the peaks and valleys? Anesthesiology 1987; 67: 1–2
- 47 Mancia G, Parati G, Pomidossi G, Grassi G, Casadei R, Zanchetti A. Alerting reaction and rise in blood pressure during measurement by physician and nurse. *Hypertension* 1987; 9: 209–15
- 48 Mangano DT, Hollenberg M, Fegert G, et al. Perioperative myocardial ischemia in patients undergoing noncardiac surgery—I: Incidence and severity during the 4 day perioperative period. The Study of Perioperative Ischemia (SPI) Research Group. J Am Coll Cardiol 1991; 17: 843–50
- 49 Mangano DT, Layug EL, Wallace A, Tateo I. Effect of atenolol on mortality and cardiovascular morbidity after noncardiac surgery. Multicenter Study of Perioperative Ischemia Research Group. N Engl | Med 1996; 335: 1713–20
- 50 O'Brien E, Coats A, Owens P, et al. Use and interpretation of ambulatory blood pressure monitoring: recommendations of the British hypertension society. BMJ 2000; 320: 1128–34
- 51 O'Brien E, Staessen JA. Critical appraisal of the JNC VI, WHO/ ISH and BHS guidelines for essential hypertension. Expert Opin Pharmacother 2000; 1: 675–82
- 52 O'Connell D, Glasziou P, Hill S, Sarunac J, Lowe J, Henry H. Results of clinical trials and systematic reviews: to whom do they apply? In: Stevens A, Abrams K, Brazier J, Fitzpatrick R, Lilford R, eds. The Advanced Handbook of Methods in Evidence Based Healthcare. London: Sage Publications, 2001; 56–72
- 53 Ombrellaro MP, Dieter RA, 3rd, Freeman M, Stevens SL, Goldman MH. Role of dipyridamole myocardial scintigraphy in carotid artery surgery. J Am Coll Surg 1995; 181: 451–8
- 54 Pasternack PF, Grossi EA, Baumann FG, et al. Silent myocardial ischemia monitoring predicts late as well as perioperative cardiac events in patients undergoing vascular surgery. J Vasc Surg 1992; 16: 171–9
- 55 Perloff D, Sokolow M. Ambulatory blood pressure: mortality and morbidity. J Hyperten Suppl 1991; 9: S31–3
- 56 Pickering TG, Coats A, Mallion JM, Mancia G, Verdecchia P. Blood pressure monitoring. Task force V: white-coat hypertension. Blood Press Monit 1999: 4: 333–41
- 57 Poldermans D, Boersma E, Bax JJ, et al. The effect of bisoprolol on perioperative mortality and myocardial infarction in high-risk patients undergoing vascular surgery. Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echocardiography Study Group. N Engl | Med 1999; 341: 1789–94
- 58 Poldermans D, Fioretti PM, Boersma E, et al. Dobutamineatropine stress echocardiography in elderly patients unable to perform an exercise test. Hemodynamic characteristics, safety, and prognostic value. Arch Intern Med 1994; 154: 2681–6
- 59 Prys-Roberts C, Foex P, Biro GP, Roberts JG. Studies of anaesthesia in relation to hypertension. V. Adrenergic betareceptor blockade. Br J Anaesth 1973; 45: 671–81
- 60 Prys-Roberts C, Foex P, Greene LT, Waterhouse TD. Studies of anaesthesia in relation to hypertension. IV. The effects of artificial ventilation on the circulation and pulmonary gas exchanges. Br J Anaesth 1972; 44: 335–49
- 61 Prys-Roberts C, Greene LT, Meloche R, Foex P. Studies of anaesthesia in relation to hypertension. II. Haemodynamic consequences of induction and endotracheal intubation. Br J Anaesth 1971; 43: 531–47
- 62 Prys-Roberts C, Meloche R, Foex P. Studies of anaesthesia in

- relation to hypertension. I. Cardiovascular responses of treated and untreated patients. Br | Anaesth 1971; 43: 122–37
- 63 Ramsay LE, Williams B, Johnston GD, et al. British Hypertension Society guidelines for hypertension management 1999: summary. BMI 1999; 319: 630–5
- 64 Rao TL, Jacobs KH, El Etr AA. Reinfarction following anesthesia in patients with myocardial infarction. Anesthesiology 1983; 59: 499–505
- 65 Redon J, Campos C, Narciso ML, Rodicio JL, Pascual JM, Ruilope LM. Prognostic value of ambulatory blood pressure monitoring in refractory hypertension: a prospective study. *Hypertension* 1998; 31: 712–8
- 66 Reich DL, Bennett-Guerrero E, Bodian CA, Hossain S, Winfree W, Krol M. Intraoperative tachycardia and hypertension are independently associated with adverse outcome in noncardiac surgery of long duration. Anesth Analg 2002; 95: 273–7
- 67 Riles TS, Kopelman I, Imparato AM. Myocardial infarction following carotid endarterectomy: a review of 683 operations. Surgery 1979; 85: 249–52
- 68 Rodgers A, Walker N, Schug S, et al. Reduction of postoperative mortality and morbidity with epidural or spinal anaesthesia: results from overview of randomised trials. BMJ 2000; 321: 1493
- 69 Shah KB, Kleinman BS, Rao TL, Jacobs HK, Mestan K, Schaafsma M. Angina and other risk factors in patients with cardiac diseases undergoing noncardiac operations. *Anesth Analg* 1990; 70: 240–7
- 70 Sicari R, Picano E, Lusa AM, et al. The value of dipyridamole echocardiography in risk stratification before vascular surgery. A multicenter study. The EPIC (Echo Persantine International Study) Group–Subproject: risk stratification before major vascular surgery. Eur Heart J 1995; 16: 842–7
- 71 Sprague HB. The heart in surgery. An analysis of the results of surgery on cardiac patients during the past ten years at the Massachusetts General Hospital. Surg Gynecol Obstet 1929; 49: 54–8

- 72 Sprung J, Abdelmalak B, Gottlieb A, et al. Analysis of risk factors for myocardial infarction and cardiac mortality after major vascular surgery. Anesthesiology 2000; 93: 129–40
- 73 Stamler J, Dyer AR, Shekelle RB, Neaton J, Stamler R. Relationship of baseline major risk factors to coronary and all-cause mortality, and to longevity: findings from long-term follow-up of Chicago cohorts. Cardiology 1993; 82: 191–222
- 74 Stamler J, Stamler R, Neaton JD. Blood pressure, systolic and diastolic, and cardiovascular risks. US population data. Arch Intern Med 1993; 153: 598–615
- 75 Steen PA, Tinker JH, Tarhan S. Myocardial reinfarction after anesthesia and surgery. JAMA 1978; 239: 2566-70
- 76 Stevens A, Abrams K. Consensus, reviews and meta-analysis. In: Stevens A, Abrams K, Brazier J, Fitzpatrick R, Lilford R, eds. Methods in Evidence Based Healthcare. London: Sage, 2001; 367–9
- 77 Stratmann HG, Younis LT, Wittry MD, Amato M, Mark AL, Miller DD. Dipyridamole technetium 99m sestamibi myocardial tomography for preoperative cardiac risk stratification before major or minor nonvascular surgery. Am Heart J 1996; 132: 536–41
- 78 Varma MK, Puri GD, Chari P, Verma JS, Kohli KK. Perioperative myocardial infarction in coronary artery disease patients and 'atrisk' for coronary artery disease patients undergoing non-cardiac surgery. Natl Med J India 1996; 9: 214–7
- 79 Varon J, Marik PE. The diagnosis and management of hypertensive crises. Chest 2000; 118: 214–27
- 80 Verdecchia P, Schillaci G, Borgioni C, Ciucci A, Porcellati C. White-coat hypertension. Lancet 1996; 348: 1444–5
- 81 vonKnorring J. Postoperative myocardial infarction: a prospective study in a risk group of surgical patients. Surgery 1981; 90: 55–60
- **82** Weksler N, Klein M, Szendro G, et al. The dilemma of immediate preoperative hypertension: to treat and operate, or to postpone surgery? *J Clin Anesth* 2003; **15**: 179–83

Editorial II

Preoperative hypertension: remain wary? 'Yes'—cancel surgery? 'No'

How often have we asked ourselves: shall I go ahead and anaesthetize this patient with uncontrolled hypertension, or should I postpone surgery until the arterial pressure is controlled? Does the benefit of preoperative arterial pressure control justify the inconvenience and financial consequences of postponing surgery? Are patients with uncontrolled hypertension at an increased perioperative risk? Are there any data on which I can base my decision? These and many other questions are addressed in the comprehensive review by Howell, Sear and Foëx in this issue of the Journal.¹

Hypertension affects one billion individuals worldwide,² and is endemic in the western world, particularly in the elderly.³ Hypertension represents a major risk factor for

coronary artery disease, ⁴ congestive heart failure, ⁵ dementia, ⁶ and renal and cerebrovascular disease, ⁷ and is associated with dyslipidaemia, diabetes, and obesity. ⁷ The higher the arterial pressure, the higher the risk of myocardial infarction, heart failure, stroke, or kidney disease. Between the age of 40 and 70 yr, for each increment of 20 mm Hg in systolic or 10 mm Hg in diastolic arterial pressure, the chance of developing cardiovascular disease doubles across the arterial pressure range from 115/75 to 185/115 mm Hg. ⁸ Therefore, the need for tight arterial pressure control and life-long treatment is undisputed.

In contrast, in the perioperative setting, the situation is less clear. The extensive literature review and meta-analysis of 30 observational studies by Howell and colleagues¹

concludes that the likelihood of experiencing an adverse perioperative cardiac event is, on average, 1.31-fold (95% confidence interval 1.13-1.51) higher in hypertensive patients than in normotensive patients. Although this difference in outcome between hypertensive and normotensive individuals is statistically significant, it is of questionable clinical relevance. First, for clinical purposes, the mean odds ratio and the 95% confidence interval are very low. Second, the significant heterogeneity between studies makes effective correction for confounding variables almost impossible. Although there seems to be a tendency for an increased incidence of perioperative haemodynamic instability, myocardial ischaemia and cardiac arrhythmias in patients with severe hypertension (systolic blood pressure >180 mm Hg, diastolic blood pressure >110 mm Hg), even for this patient population, existing data do not unequivocally support the hypothesis that postponing surgery to control arterial pressure will improve perioperative cardiac outcome.

In essence, the result of the meta-analysis by Howell and colleagues¹ casts considerable doubt that the perioperative outcome is worse in hypertensive than in normotensive patients. Therefore, in most clinical situations, cancellation of surgery for the sole reason of uncontrolled hypertension hardly seems a defensible option. This is in accordance with recent guidelines of the American College of Cardiology and the American Heart Association,⁹ and similar recommendations¹⁰ in which uncontrolled systemic hypertension *per se* is considered only a minor risk factor that does not affect overall perioperative management.

However, are we really justified in interpreting the data as showing that there is never any reason for cancelling surgery because of uncontrolled hypertension? We have to acknowledge that we lack large-scale trials that include a sufficient number of patients with severe hypertension to allow valid statistical analysis and thus for us to draw conclusions in this patient population. The results of investigations that failed to identify mild and moderate hypertension as a predictor of adverse perioperative outcome may not be transferable to the population with poorly controlled severe hypertension. Furthermore, the initial diagnosis of hypertension might have triggered a search for coronary artery disease. If found to be present, this would counteract the impact of hypertension alone in studies that used multivariate models. It therefore seems important to preoperatively differentiate between isolated hypertension and hypertension associated with coronary artery disease.

Why should anaesthetists remain wary of hypertension? For at least three reasons: (i) hypertensive patients tend to be more haemodynamically unstable and prone to myocardial ischaemia in the perioperative period. Several studies have demonstrated a significant association between perioperative myocardial ischaemia and postoperative ischaemic cardiac events, such as unstable angina, nonfatal myocardial infarction, and cardiac death. (ii)

Hypertension is a major risk factor for coronary artery disease, ^{4 10} congestive heart failure, ⁵ and renal and cerebrovascular disease. ⁷ Any of these factors increase the likelihood of perioperative myocardial infarction or death. ¹⁴ And (iii), hypertension is associated with dyslipidaemia, diabetes, and obesity, ⁷ and the side-effects of drugs needed to treat these diseases. ^{15 16}

How can we safely anaesthetize hypertensive patients? Essential elements of perioperative management include careful preoperative evaluation, tight perioperative arterial pressure and heart rate control, cardiac protection, and a well trained, experienced and dedicated anaesthetist.

Preoperatively, it may be helpful to contact the referring general practitioner to obtain more realistic arterial pressure values than the ones measured at hospital admission, which might overestimate the long-term arterial pressure level (referred to as 'white coat' or 'isolated office hypertension'). Hypertension-induced target organ damage should be sought and, if present, evaluated and appropriately treated. Assessment of physical exercise tolerance is crucial. 9 10 17 In special situations, postponement of surgery in hypertensive patients may be justified to allow for additional preoperative cardiac testing. In the context of isolated hypertension, however, additional testing is rarely indicated and should only be considered in patients scheduled for high-risk surgery (e.g. major vascular surgery). If in addition to an elevated arterial pressure, signs of coronary artery (e.g. ischaemic electrocardiographic changes) or renal disease (e.g. elevated serum creatinine) are discovered, coupled with poor exercise tolerance and an intermediate- or high-risk surgical procedure, then additional preoperative cardiac testing should also be considered. 9 10 However, such testing should only be performed if the results are likely to have an impact on perioperative management (e.g. before coronary revascularization, modification of perioperative monitoring, changes in medical management).

Perioperative arterial pressure and heart rate control is essential in hypertensive patients. While hypertensive peaks need to be avoided, profound (relative) hypotension, especially when associated with baroreflex-mediated tachycardia, can be equally detrimental. Interestingly, in a study of 676 consecutive patients, hypertension at hospital admission was not associated with perioperative cardiac complications, but severe decreases in intraoperative arterial pressure (decrease to <50% of preoperative levels or by >33% for >10 min) was indeed an independent predictor of perioperative adverse advents. Maintaining arterial pressure perioperatively at 70–100% of baseline and avoiding tachycardia is a key factor in the optimal management of hypertensive surgical patients.

As hypertension is strongly associated with cardiovascular disease, and as cardiac events are the main cause of adverse perioperative outcome, the perioperative anaesthetic management of hypertensive patients must place particular emphasis on cardiac protection. This may be achieved by perioperative β -blockade, ¹⁹ and possibly by pharmacological preconditioning. ¹⁶ ^{20–22}

Two major outcome studies have demonstrated a reduction in mortality in patients with or at risk of coronary artery disease by perioperative β -blocker therapy. 23 24 The study populations included a significant number of hypertensive patients. Although both investigations have been criticized because of considerable methodological limitations, 25 the results, nevertheless, strongly suggest that hypertensive patients with the associated high incidence of coronary artery disease are likely to benefit from aggressive perioperative treatment with β -blockers, preferably β -1 selective antagonists. 17 19 25 Ideally, the referring general practitioner is contacted well ahead of the operation, so that β -blockade may be commenced days to weeks before the surgical intervention. 19

Pharmacological preconditioning by inhalational anaesthetics may become another means of perioperative cardiac protection. $^{16\,20\,21}$ Inhalational anaesthetics seem to improve tolerance of myocardial ischaemia by acting as openers of mitochondrial and sarcolemmal ATP-regulated potassium (K_ATP) channels. $^{16\,20\,21}$ This may be of particular benefit in hypertensive patients given the high prevalence of associated coronary artery disease 4 and their vulnerability to perioperative myocardial ischaemia. 11 In contrast, as sulphonylurea hypoglycaemic agents close K_{ATP} channels to increase insulin release from pancreatic islet cells, they may prevent anaesthetics from exerting pharmacological preconditioning and associated cardiac protection. It is thus advisable to discontinue such drugs 1–2 days before elective surgery. 15

The review by Howell and colleagues¹ implies that patients are unlikely to die perioperatively from a preoperatively elevated arterial pressure level *per se* but, more likely, from underlying hypertension-associated comorbidities and, possibly, from inadequate perioperative management because of lack of understanding of the pathophysiology of hypertension. Clearly, the difference between an adverse and favourable outcome can be achieved not by treatment of numbers (in this case arterial pressure values), but rather by the appropriate perioperative management of the disease entity. Obviously, hypertension is only one of many risk factors that determine perioperative management and outcome—and, apparently, not the most important one.^{9 10}

There is general agreement based on the evidence presented by Howell and colleagues¹ that patients with mild and moderate hypertension and no evidence of coronary artery disease or end-organ damage may safely undergo surgery without delay. In contrast, for patients with severe hypertension, the data are insufficient to allow an unequivocal recommendation as to what constitutes the optimal approach. Any recommendation to postpone elective surgery for the purpose of preoperative arterial pressure control must be balanced against the urgency and benefit of the planned operation; must take into account that arterial

pressure should be corrected slowly, and that up to 2 months may be required to reverse some of the hypertension-induced cardiovascular changes;¹⁴ and must acknowledge the fact that data are lacking to support such practice.

Chronic hypertension may go undetected for a long time. It may well be found for the first time during routine preoperative assessment. Modern anaesthesia provided by a well trained, experienced and dedicated anaesthetist offers sufficient perioperative cardiac protection to make cancellation of surgery for the sole purpose of controlling preoperative hypertension unnecessary under most circumstances. Appropriate evaluation and intervention can be expected to improve perioperative and long-term outcome. When confronted with uncontrolled preoperative hypertension, we need to remain wary but not become unduly alarmed.

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References

- I Howell SJ, Sear JW, Foëx P. Hypertension, hypertensive heart disease and perioperative cardiac risk. Br J Anaesth 2004; 92: 570-83
- 2 Chobanian AV, Bakris GL, Black HR, et al. The seventh report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure: the JNC 7 report. JAMA 2003; 289: 2560–72
- 3 Priebe HJ. The aged cardiovascular risk patient. Br J Anaesth 2000; 85: 763–78
- 4 Prevention of stroke by antihypertensive drug treatment in older persons with isolated systolic hypertension. Final results of the Systolic Hypertension in the Elderly Program (SHEP). SHEP Cooperative Research Group. JAMA 1991; 265: 3255–64
- 5 Levy D, Larson MG, Vasan RS, Kannel WB, Ho KK. The progression from hypertension to congestive heart failure. JAMA 1996; 275: 1557–62
- 6 Forette F, Seux ML, Staessen JA, et al. Prevention of dementia in randomised double-blind placebo-controlled Systolic Hypertension in Europe (Syst-Eur) trial. Lancet 1998; 352: 1347-51
- 7 Kannel WB. Blood pressure as a cardiovascular risk factor: prevention and treatment. JAMA 1996; 275: 1571–6
- 8 Lewington S, Clarke R, Qizilbash N, Peto R, Collins R. Agespecific relevance of usual blood pressure to vascular mortality: a

- meta-analysis of individual data for one million adults in 61 prospective studies. Lancet 2002; **360**: 1903–13
- 9 Eagle KA, Berger PB, Calkins H, et al. ACC/AHA guideline update for perioperative cardiovascular evaluation for noncardiac surgery—executive summary a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1996 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery). Circulation 2002; 105: 1257–67
- 10 Chassot PG, Delabays A, Spahn DR. Preoperative evaluation of patients with, or at risk of, coronary artery disease undergoing non-cardiac surgery. Br J Anaesth 2002; 89: 747–59
- 11 Prys-Roberts C, Meloche R, Foëx P. Studies of anaesthesia in relation to hypertension. I. Cardiovascular responses of treated and untreated patients. Br J Anaesth 1971; 43: 122–37
- 12 Mangano DT, Browner WS, Hollenberg M, London MJ, Tubau JF, Tateo IM. Association of perioperative myocardial ischemia with cardiac morbidity and mortality in men undergoing noncardiac surgery. The Study of Perioperative Ischemia Research Group. N Engl J Med 1990; 323: 1781–8
- 13 Landesberg G, Luria MH, Cotev S, et al. Importance of longduration postoperative ST-segment depression in cardiac morbidity after vascular surgery. Lancet 1993; 341: 715–19
- 14 Fleisher LA. Preoperative evaluation of the patient with hypertension. JAMA 2002; 287: 2043–6
- 15 Gu W, Pagel PS, Warltier DC, Kersten JR. Modifying cardiovascular risk in diabetes mellitus. Anesthesiology 2003; 98: 774–9
- 16 Warltier DC, Kersten JR, Pagel PS, Gross GJ. Editorial view: anesthetic preconditioning: serendipity and science. Anesthesiology 2002; 97: 1–3
- 17 Lee TH. Reducing cardiac risk in noncardiac surgery. N Engl J Med 1999; 341: 1838–40

- 18 Goldman L, Caldera DL. Risks of general anesthesia and elective operation in the hypertensive patient. Anesthesiology 1979; 50: 285–92
- 19 Zaugg M, Schaub MC, Pasch T, Spahn DR. Modulation of beta-adrenergic receptor subtype activities in perioperative medicine: mechanisms and sites of action. Br J Anaesth 2002; 88: 101–23
- 20 Zaugg M, Lucchinetti E, Uecker M, Pasch T, Schaub MC. Anaesthetics and cardiac preconditioning: Part I Signalling and cytoprotective mechanisms. Br J Anaesth 2003; 91: 551–65
- 21 Zaugg M, Lucchinetti E, Garcia C, Pasch T, Spahn DR, Schaub MC. Anaesthetics and cardiac preconditioning: Part II Clinical implications. Br J Anaesth 2003; 91: 566–76
- 22 van der Linden PJ, Daper A, Trenchant A, De Hert SG. Cardioprotective effects of volatile anesthetics in cardiac surgery. *Anesthesiology* 2003; 99: 516–17
- 23 Mangano DT, Layug EL, Wallace A, Tateo I. Effect of atenolol on mortality and cardiovascular morbidity after noncardiac surgery. Multicenter Study of Perioperative Ischemia Research Group. N Engl | Med 1996; 335: 1713–20
- 24 Poldermans D, Boersma E, Bax JJ, et al. The effect of bisoprolol on perioperative mortality and myocardial infarction in high-risk patients undergoing vascular surgery. Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echocardiography Study Group. N Engl J Med 1999; 341: 1789–94
- 25 Howell SJ, Sear JW, Foëx P. Peri-operative beta-blockade: a useful treatment that should be greeted with cautious enthusiasm. *Br J Anaesth* 2001; **86**: 161–4

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