

Appendix S1. Peri-operative blood pressure medication management

Deranged blood pressure regulation is common in the peri-operative period for non-cardiac surgery. Pre-, intra- and postoperative hypotension (mean arterial pressure (MAP) < 60-70mmHg or systolic arterial pressure < 100 mmHg [1]) are all associated with a higher risk of major cardiovascular complications, acute kidney injury and all-cause mortality at 30 days [2–11]. Specific organ injury is related to the duration of hypotension [7,10,12]. However, even transient periods of systolic hypotension are associated with myocardial injury and increased mortality risk [11]. Postoperative hypotension is a common and associated with excess morbidity and mortality, especially if occurring for a prolonged period or on days 1-4 postoperatively [10].

Periods of elevated intra-operative blood pressure during non-cardiac surgery is not as strongly associated with excess postoperative morbidity and mortality as hypotension [1,11]. However, an upper pressure limit at which therapy should be commenced, bespoke to both the patient and the surgical procedure performed, is advised.

Antihypertensive agents are an important risk factor in the development of intra-operative hypotension and the subsequent adverse effects on vital organs. With more patients presenting for surgery on multiple antihypertensive agents, careful consideration of drug continuation or cessation is required.

When to stop and when to restart specific antihypertensive treatments

Beta-blockers

Patients on long-term beta-blocker therapy prior to surgery should continue their current treatment in the peri-operative period [13–15]. Omission of beta-blocker treatment in patients who are hypertensive with high-risk concomitant indications (e.g. congestive cardiac failure or recent myocardial infarction) is associated with increased postoperative mortality and interruption of therapy for > 2 days may double peri-operative risk of atrial fibrillation [13,15–19]. Patients on beta-blockers for uncomplicated hypertension are frequently on multiple agents as beta-blockade is not first-line therapy. For these lower-risk individuals on ≥ 2 antihypertensives (including a beta-blocker) evidence suggests possible increased harm with therapy continuation over the peri-operative period [20]. If held, caution should be exercised when restarting at the chronic pre-operative dose if no contraindications have arisen [3,20]. Use of a smaller titrated dose may be more appropriate to avoid hypotension and bradycardia. Beta-blockers should not be initiated immediately before surgery for risk reduction due to the associated increased risk of stroke and mortality [3].

Angiotensin-converting enzyme inhibitors and angiotensin-receptor blockers (ACEI/ARB)

Renin-angiotensin-aldosterone system (RAAS) inhibitors are the first-line therapy for hypertension [21]. For patients having non-cardiac surgery, it has become common practice to discontinue ACEI/ARB inhibitors peri-operatively to limit the (possible) increased risk of intra-operative hypotension and associated postoperative complications [22–26]. There has been conflicting data on postoperative morbidity and mortality outcomes from continuing therapy, leading to equipoise regarding RAAS inhibitor use guidance in the peri-operative setting. Several recent randomised controlled trials showed comparable postoperative outcomes whether ACEI/ARBs were continued or discontinued in the peri-operative period [27,28]. Patients continuing ACEI/ARB therapy had higher incidences of intra-operative hypotension but with a negligible difference in duration of hypotension [27], whilst those who stopped medications had an increase in postoperative hypertensive events [28]. Because these recent studies suggest

that there is no additional risk in continuing ACEI/ARB, we now recommend that they should be continued throughout the peri-operative period.

Patients living with obesity having specialist bariatric surgery should continue all routine antihypertensive medications pre-operatively (i.e. not stop ACEI or ARB). Similarly, if concomitant heart failure is present and stable, peri-operative continuation of ACEI/ARB should be considered [13]. If the decision is to omit, ACEI/ARB should be held 24 h prior to surgery with therapy recommenced within 48 h of surgery (or as soon as reasonable) [13,14]. Delayed or long-term omission of ACEI/ARBs has been associated with increased postoperative mortality [29,30]. If there is a postoperative increase in serum creatine or if hypotension is present, then caution restarting therapy is warranted.

Renin inhibitors (e.g. aliskiren) and angiotensin receptor-neprilysin inhibitors (e.g. sacubitril/valsartan) are recommended to be held on day of surgery due to the risk of profound intra-operative hypotension [31].

Calcium channel antagonists

Little evidence exists regarding the peri-operative management of calcium channel blockers prescribed for hypertension. The limited evidence from small RCTs suggest that continuation of calcium channel blockers may be associated with improved outcomes [32,33]. Consensus guidance recommend continuing calcium channel blockers prescribed for hypertension during the peri-operative period [14,15]. However, withholding administration on day of surgery to avoid peri-operative hypotension may also be considered [13].

Diuretics

Diuretics are used commonly in the management of both hypertension and heart failure. Definitive evidence that thiazide diuretics cause harm peri-operatively is lacking [20,31]. When used to treat hypertension, diuretic therapy should generally continue but may be transiently discontinued on the day of surgery and resumed orally when possible [13,14,31] on a per-patient basis (particularly for loop diuretics).

Vigilance for possible peri-operative electrolyte disturbance, such as hypokalaemia, should be exercised for all patients receiving diuretics. Little evidence exists to guide postoperative reintroduction; consideration of electrolytes, blood pressure and fluid status should all contribute to the assessment.

Alpha-blockers

This less commonly used class of antihypertensive have insufficient evidence for clear guidance in the peri-operative period; it is generally accepted to continue therapy on the day of surgery. Chronic alpha-2 agonist (e.g. clonidine) usage should not be acutely omitted as this may cause rebound hypertension.

Sodium–glucose co-transporter-2 (SGLT2) inhibitors

We have not considered this class of drugs as although they have a blood pressure lowering effect, they are not used routinely for this purpose and their management in the peri-operative setting is covered by other guidelines [34]

References

1. Sessler DI, Bloomstone JA, Aronson S, et al. Perioperative Quality Initiative consensus statement on intraoperative blood pressure, risk and outcomes for elective surgery. *Br J Anaes* 2019;122:563–74.
2. Venkatesan S, Myles PR, Manning HJ et al. Cohort study of preoperative blood pressure and risk of 30-day mortality after elective non-cardiac surgery. *British journal of anaesthesia* 2017;119:174–174.
3. Devereaux PJ, Yang H, Yusuf S, et al. Effects of extended-release metoprolol succinate in patients undergoing non-cardiac surgery (POISE trial): a randomised controlled trial. *The Lancet* 2008;371:1839–47.
4. Mascha EJ, Yang D, Weiss S, Sessler DI. Intraoperative mean arterial pressure variability and 30-day mortality in patients having noncardiac surgery. *Anesthesiology* 2015;123:79–91.
5. Walsh M, Devereaux PJ, Garg AX, et al. Relationship between intraoperative mean arterial pressure and clinical outcomes after noncardiac surgery: toward an empirical definition of hypotension. *Anesthesiology* 2013;119:507–15.
6. Monk TG, Bronsert MR, Henderson WG, et al. Association between intraoperative hypotension and hypertension and 30-day postoperative mortality in noncardiac surgery. *Anesthesiology* 2015;123:307–19.
7. Sun LY, Wijeyesundera DN, Tait GA, Beattie WS. Association of intraoperative hypotension with acute kidney injury after elective noncardiac surgery. *Anesthesiology* 2015;123:515–23.
8. van Waes J, Van Klei WA, Wijeyesundera DN, Van Wolfswinkel L, Lindsay TF, Beattie WS. Association between intraoperative hypotension and myocardial injury after vascular surgery. *Anesthesiology* 2016;124:35–44.
9. Salmasi V, Maheshwari K, Yang D, et al. Relationship between intraoperative hypotension, defined by either reduction from baseline or absolute thresholds, and acute kidney and myocardial injury after noncardiac surgery. *Anesthesiology* 2017;126:47–65.
10. Sessler DI, Meyhoff CS, Zimmerman NM, et al. Period-dependent associations between hypotension during and for four days after noncardiac surgery and a composite of myocardial infarction and death: a substudy of the POISE-2 trial. *Anesthesiology* 2018;128:317–27.
11. Abbott TEF, Pearse RM, Archbold RA et al. A prospective international multicentre cohort study of intraoperative heart rate and systolic blood pressure and myocardial injury after noncardiac surgery: results of the VISION study. *Anesth Analg* 2018;126:1936–45.
12. Stapelfeldt WH, Yuan H, Dryden JK, et al. The SLUScore: a novel method for detecting hazardous hypotension in adult patients undergoing noncardiac surgical procedures. *Anesth Analg* 2017;124:1135–52.
13. Halvorsen S, Mehilli J, Cassese S, et al. 2022 ESC Guidelines on cardiovascular assessment and management of patients undergoing non-cardiac surgery Developed by the task force for cardiovascular assessment and management of patients undergoing non-cardiac surgery of the European Society of Cardiology (ESC) Endorsed by the European Society of Anaesthesiology and Intensive Care (ESAIC). *Eur Heart J* 2022;43(39).
14. Sanders RD, Hughes F, Shaw A et al. Perioperative Quality Initiative consensus statement on preoperative blood pressure, risk and outcomes for elective surgery. *British Journal of Anaesthesia* 2019;122:552–62.
15. Whelton PK, Carey RM, Aronow WS et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A

- Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol* 2018;71:e127–248.
16. London MJ, Kwan Hur, Schwartz GG, Henderson WG. Association of perioperative beta-blockade with mortality and cardiovascular morbidity following major noncardiac surgery. *JAMA* 2013;309:1704.
 17. Kertai MD, Cooter M, Pollard RJ et al. Is compliance with surgical care improvement project cardiac measures for perioperative [beta]-blockers associated with reduced incidence of mortality and cardiovascular-related critical quality indicators after noncardiac surgery? *Anesth Analg* 2018;126:1829.
 18. Kwon S, Thompson R, Florence M, et al. Beta-blocker continuation after noncardiac surgery: a report from the surgical care and outcomes assessment program. *Archives of Surgery* 2012;147:467.
 19. Wallace AW, Au S, Cason BA. Association of the pattern of use of perioperative β -blockade and postoperative mortality. *Anesthesiology* 2010;113:794–805.
 20. Jørgensen ME, Hlatky MA, Køber L et al. β -Blocker-associated risks in patients with uncomplicated hypertension undergoing noncardiac surgery. *JAMA Intern Med* 2015;175:1–9.
 21. Lewis P, George J, Kapil V, Poulter NR, Partridge S, Goodman J, Faconti L, McCormack T, Wilkinson IB. Adult hypertension referral pathway and therapeutic management: British and Irish Hypertension Society position statement. *J Hum Hypertens* 2024; 38:3-7. <https://doi.org/10.1038/s41371-023-00882-2>
 22. Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: executive summary. *Journal of Nuclear Cardiology*. 2015;22:162–215.
 23. Nielson E, Hennrikus E, Lehman E, Mets B. Angiotensin axis blockade, hypotension, and acute kidney injury in elective major orthopedic surgery. *J Hosp Med* 2014;9:283–8.
 24. Zainudheen A, Scott IA, Caney X. Association of renin angiotensin antagonists with adverse perioperative events in patients undergoing elective orthopaedic surgery: a case-control study. *Intern Med J* 2017;47:999–1005.
 25. Hollmann C, Fernandes NL, Biccard BM. A systematic review of outcomes associated with withholding or continuing angiotensin-converting enzyme inhibitors and angiotensin receptor blockers before noncardiac surgery. *Anesth Analg* 2018;127:678–87.
 26. Roshanov PS, Rochweg B, Patel A, et al. Withholding versus continuing angiotensin-converting enzyme inhibitors or angiotensin ii receptor blockers before noncardiac surgery: an analysis of the Vascular events In noncardiac Surgery patlents cOhort evaluationN prospective cohort. *Anesthesiology* 2017;126:16–27.
 27. Legrand M, Falcone J, Cholley B, et al. Continuation vs discontinuation of renin-angiotensin system inhibitors before major noncardiac surgery: the Stop-or-Not randomized clinical trial. *JAMA* 2024;332:970–978.
 28. Ackland GL, Patel A, Abbott TEF, et al. Discontinuation vs. continuation of renin-angiotensin system inhibition before non-cardiac surgery: the SPACE trial. *European Heart Journal* 2024; 45: 1146-55
 29. Lee SM, Takemoto S, Wallace AW. Association between withholding angiotensin receptor blockers in the early postoperative period and 30-day mortality: a cohort study of the Veterans Affairs healthcare system. *Anesthesiology* 2015;123:288–306.
 30. Mudumbai SC, Takemoto S, Cason BA, Au S, Upadhyay A, Wallace AW. Thirty-day mortality risk associated with the postoperative non-resumption of angiotensin-converting enzyme inhibitors: A retrospective study of the Veterans Affairs healthcare system. *J Hosp Med* 2014;9:289–96.

31. Sahai SK, Balonov K, Bentov N, et al. Preoperative management of cardiovascular medications: A Society for Perioperative Assessment and Quality Improvement (SPAQI) consensus statement. *Mayo Clin Proc* 2022;97:1734–51.
32. Wijesundera DN, Beattie WS. Calcium channel blockers for reducing cardiac morbidity after noncardiac surgery: a meta-analysis. *Anesth Analg* 2003;97:634–41.
33. Wijesundera DN, Beattie WS, Rao V, Ivanov J, Karkouti K. Calcium antagonists are associated with reduced mortality after cardiac surgery: a propensity analysis. *J Thorac Cardiovasc Surg.* 2004;127:755–62. 34.
34. El-Boghdady K, Dhese J, Fabb P, et al. Elective peri-operative management of adults taking glucagon-like peptide-1 receptor agonists, glucose-dependent insulinotropic peptide agonists and sodium-glucose cotransporter-2 inhibitors: a multidisciplinary consensus statement. *Anaesthesia* 2025; <https://doi.org/10.1111/anae.16541>