

CASE REPORT

Challenges in Perioperative Fluid Management and Anticoagulant Therapy in a Woman with Cardio-Pulmonary-Renal Disease Diagnosed with Preinvasive Breast Carcinoma

LEE ZQ¹, NORLIA A¹, SYARIFAH NOOR NAZIHAH SM², TAN KL³

¹Department of Surgery, ²Department of Anaesthesiology & Intensive Care, Faculty of Medicine, Universiti Kebangsaan Malaysia, Jalan Yaacob Latif, Bandar Tun Razak, 56000 Cheras, Kuala Lumpur, Malaysia

³The National Heart Institute, Kuala Lumpur, Malaysia / Columbia Asia Hospital, Seremban.

ABSTRAK

Seorang wanita yang telah lanjut usia dengan barah payudara prainvasif, fibrilasi atrial, fistula arteri koronari-arteri pulmonari, hipertensi pulmonari dan nefropati diabetik Tahap 4 telah menjalani mastektomi dan biopsi sentinel nodus limfa. Mengurus keseimbangan cecair dan rawatan antikoagulan perioperatifnya adalah sesuatu yang mencabar. Menghidap barah, fibrilasi atrial dan kurang hidrasi akan meningkatkan risiko hiperkoagulasi. Walau bagaimanapun, cecair yang berlebihan pula boleh mengakibatkan edema pulmonari yang akan mengurangkan lagi oksigenasinya kerana telah mempunyai hipertensi pulmonari. Pemberhentian rawatan anti-koagulan juga meningkatkan risiko hiperkoagulasi. Terapi antikoagulan sebaliknya meningkatkan risiko pendarahan tempat pembedahan yang mungkin memerlukan bius am sekali lagi untuk mengenalpasti dan memberhentikan punca pendarahan dan mengeluarkan ketulan darah. Himpunan ketulan darah juga akan meningkatkan risiko jangkitan kuman, lebih-lebih lagi kerana dia menghidap kencing manis. Terapi antikoagulannya (rivaroxaban) telah diberhentikan 4 hari sebelum pembedahan. Peratus pengepaman jantungnya ialah 50%, dengan mempunyai masalah pengepaman diastolik Gred 2 dan TAPSE 0.6 cm. Skor CHA₂D₂-VASc beliau ialah 5. Sebelum pembedahan, kanulasi intraarterinya telah disambung ke pegasan FloTrac™ dan pemantau EV1000™. Pengurusan cecairnya telah dipantau menggunakan terapi cecair berpandu matlamat ('goal-directed', GD). Pembedahan berjaya dilaksanakan dan terapi antikoagulannya telah dimulakan semula 14 hari selepas pembedahan.

Address for correspondence and reprint requests: Professor Dr. Norlia Abdullah. Department of Surgery, Faculty of Medicine, Universiti Kebangsaan Malaysia, Jalan Yaacob Latif, Bandar Tun Razak, 56000 Cheras, Kuala Lumpur, Malaysia. Tel: +603-9145 5795 Email: norlia@ppukm.ukm.edu.my

Kata kunci: barah payudara, fibrilasi atrial, hiperkoagulasi, hipertensi pulmonari, mastektomi, nefropati, pendarahan

ABSTRACT

An elderly woman with preinvasive breast cancer, atrial fibrillation, coronary artery-pulmonary artery fistula, pulmonary hypertension and Stage 4 diabetic nephropathy underwent a mastectomy and sentinel lymph node biopsy. Managing her perioperative fluid balance and anticoagulation treatment were challenging. Having a malignancy, atrial fibrillation plus underhydration will increase her risk of hypercoagulation. However, fluid overload will lead to pulmonary oedema which will decrease her oxygenation further in pulmonary hypertension. Cessation of anticoagulation also increased the risk of hypercoagulation. Anticoagulant therapy increases the risk of a perioperative wound haematoma, which may require another general anaesthesia for identification and arrest of the bleeding source and haematoma evacuation. A haematoma will also increase the risk of surgical site infection; especially as a diabetic. Her anticoagulant therapy (rivaroxaban) was stopped four days preoperatively. Her ejection fraction was 50%, with Grade II diastolic dysfunction and TAPSE 0.6 cm. Her CHA₂DS₂-VASc Score was 5. Perioperatively, intraarterial cannulation was connected to the FloTrac™ sensor and EV1000™ monitor. Her fluid management was monitored using goal directed (GD) fluid therapy. The patient underwent surgery successfully and her anticoagulant therapy was recommenced 14 days postoperatively.

Keywords: atrial fibrillation, breast cancer, haematoma, hypercoagulation, mastectomy, nephropathy, pulmonary hypertension

INTRODUCTION

Perioperative anticoagulation management in a patient with high thromboembolic risk is a challenge due to the delicate balance between haemorrhagic and thromboembolic events. This case report described the added challenge which was perioperative fluid management in an elderly woman with preinvasive breast cancer who had serious comorbidities consisting of atrial fibrillation, coronary artery-pulmonary artery fistula,

pulmonary hypertension and Stage 4 diabetic nephropathy.

CASE REPORT

A 73-year-old woman presented with a painless right breast swelling for the duration of four months associated with serous nipple discharge. Her sister was diagnosed with breast cancer at the age of 33 years old. Examination revealed a hard lump at the upper outer quadrant of the right breast measuring 4cm x 4cm. There were

no palpable axillary lymph nodes bilaterally and no contralateral breast lump. Mammogram and ultrasound showed a suspicious right breast mass BIRADS 5. A core needle biopsy was reported as ductal carcinoma in situ, intermediate grade, ER/PR negative. There was insufficient tissue for Her2 testing. The patient opted for a right mastectomy and sentinel lymph node biopsy although breast conserving surgery was offered.

She was diagnosed with atrial fibrillation and a coronary artery-pulmonary artery fistula with pulmonary arterial hypertension (PAH) 10 years ago. Her preoperative echocardiogram showed a reduced left ventricular systolic function with an estimated ejection fraction of 50% with grade II diastolic dysfunction, dilated left and right atrium and moderate tricuspid regurgitation, estimated pulmonary arterial pressure of 80/15 mmHg (Normal range 25-30/8-10 mmHg) (Klabunde 2022) with a measurement of tricuspid annular plane systolic excursion (TAPSE) of 6 mm. The TAPSE is a prognostic indicator for the assessment of disease severity and response to therapy. TAPSE of <15 mm is associated with a significantly higher risk of mortality (Galie et al. 2009), as observed in this patient.

In terms of risk of a thromboembolic event, her CHA₂DS₂-VASc Score was 5 (Range 0-9). This score is for stroke risk assessment in those with non-valvular atrial fibrillation. The letters stand for Congestive heart failure, Hypertension, Age ≥75 years, Diabetes mellitus, Stroke (double weight), Vascular disease, Age

65-74 years, Sex category (Olesen et al. 2012). Five years ago, she was also diagnosed with Stage 4 diabetic nephropathy with eGFR of 25 ml/min/1.73m², needing restriction of total daily fluid intake to only 500 cc/day. As her CHA₂DS₂-VASc score was high, one of the newer oral anticoagulants; rivaroxaban (factor Xa inhibitor) was commenced for stroke prevention in atrial fibrillation (SPAF). With renal impairment, she was prescribed rivaroxaban at a lower dose of 15 mg daily, although the standard dose was 20 mg daily.

With these comorbidities, her general anaesthetic risk was high. She was admitted four days preoperatively, for optimisation of her health status, and was co-managed by a multi-disciplinary team consisting of the primary surgical team, a cardiologist and anaesthetists. It was decided to stop her rivaroxaban on that same day. Compression Thromboembolic Deterrent (TED) stockings were worn by the patient just prior to surgery and postoperatively whilst in the hospital, to prevent lower limb venous thrombosis.

Preinduction, intraarterial cannulation was inserted and connected to the FloTrac™ sensor and EV1000™ monitor (Edwards Lifesciences, Irvine, CA) for continuous measurement of haemodynamic parameters in the intensive care unit (ICU). This is a pulse contour cardiac output monitoring that allows measurement of haemodynamic status such as cardiac index, stroke volume, stroke volume variation and systemic vascular resistance index, apart from blood pressure monitoring.

A low dose of dobutamine infusion was commenced at induction to improve her cardiac index and prevent hypotension. She underwent a two-hour operation consisting of a right mastectomy and sentinel lymph node biopsy, uneventfully. The estimated blood loss was 300 cc. She was given intravenous 900 cc crystalloids and her urine output was 300 cc. The fluids given intraoperatively were based on the maintenance of the stroke volume variation to her baseline. The general anaesthesia was reversed with Sugammadex (a modified gamma cyclodextrin), a neuromuscular blockage reversal. Sugammadex was the medication of choice to ensure adequate reversal without cardiovascular side effects (Pani et al. 2015). On the second postoperative day, she was stable, and was transferred out of the ICU to the general surgical ward. She was discharged on postoperative day 7 without any complications. Rivaroxaban was restarted one week after discharge (14th postoperative day). The delayed recommencement took into consideration a moderate to high risk of postoperative haematoma. During this 18 days' period without any anticoagulants, she did not suffer from any thromboembolic events.

DISCUSSION

This patient was deemed high risk for general anaesthesia in view of her pre-morbid status of pulmonary hypertension with high pulmonary arterial pressure. Cardiovascular monitoring system plays an important

role in optimising perioperative haemodynamic management (Vincent et al. 2015). It is important to maintain the blood pressure perioperatively to be above the pulmonary arterial pressure in order to avoid a decreased right ventricular coronary perfusion. Pulse contour cardiac output monitoring offers additional information that is important and relevant in managing this patient. The goal is to maintain adequate preload, systemic vascular resistance (SVR), and contractility in order to allow the right ventricle to maintain cardiac output. Apart from that, it is essential to prevent an increase in pulmonary vascular resistance (PVR), which may occur as a result of hypoxia, hypercarbia, acidosis, agitation, pain and hypothermia (Pritts & Pearl 2010).

It is challenging to maintain optimal perioperative fluid balance in a post-mastectomy patient with cardiac, pulmonary and renal dysfunction. However, this is important to ensure adequate intravascular volume, optimal viscosity and tissue perfusion. Administration of excessive fluid in such a patient may lead to cardiopulmonary overload with complications such as acute pulmonary oedema and respiratory failure. This in turn will give rise to an increase in the length of hospital stay, morbidity and mortality. In addition, it is also reported that the excess fluid given during the postoperative period may result in poor wound healing, with a higher risk of surgical site infection (Giglio et al. 2009; Lobo et al. 2002; Nisanevich et al. 2005). On the other hand, inadequate fluid management may increase blood

viscosity and give rise to an increased risk of thromboembolism (Al Rasyid et al. 2019).

This patient was at high risk of developing a thromboembolic event due to several risk factors: the presence of a malignancy, postoperative immobility and atrial fibrillation. With breast cancer, it is reported that the risk of ischaemic stroke increases, known as a cancer associated stroke (Dardiotis et al. 2019). This is due to the association between hypercoagulability and malignancy. The patient also had poor postoperative mobility that can cause venous stasis plus the presence of atrial fibrillation that may impair cardiac output.

Fluid management should be monitored using an objective clinical assessment. This is known as goal directed (GD) fluid therapy. One meta-analysis had shown that GD fluid therapy reduced cardiopulmonary overload complications but maintained adequate hydration and renal perfusion (Corcoran et al. 2012). In this patient, GD fluid therapy was objectively measured by stroke volume variation (SVV) using the pulse contour cardiac output monitoring. Ideally, SVV should be maintained at 10-13% to ensure adequate fluid therapy. The SVV is a more accurate indicator of fluid responsiveness than central venous pressure (Angappan et al. 2015). The measurement of SVV can be inaccurate in this patient in view of the presence of tricuspid regurgitation, but the trend of SVV can always be used to guide fluid management (Vincent et al. 2015). Clinically, the patient was monitored for adequate perfusion via

maintenance of a normal mean arterial pressure (MAP), urine output of more than 0.5 ml/kg/hr, normal arterial blood gas and normal lactate level.

Anticoagulation is prescribed for those with atrial fibrillation to minimise the risk of developing an intracardiac blood clot. Traditionally, warfarin is prescribed. However, newer anticoagulants, named Novel Oral Anticoagulants (NOACs) or Direct Oral Anticoagulants (DOACs) such as rivaroxaban, apixaban, edoxaban and dabigatran are available. The benefit of these over warfarin is that there is a standardised dosing without the need for regular blood test monitoring. The onset of action is rapid. There is also a greatly reduced need for bridging with injections whenever anticoagulation is interrupted for invasive tests, procedures or surgery. However, satisfactory renal function is required as these medications are primarily excreted via the kidneys. The NOACs are contraindicated in patients with end stage renal failure on dialysis and those with $eGFR < 15 \text{ ml/min/1.73m}^2$. However, rivaroxaban at a reduced dose may be given to those with $eGFR$ between $15\text{-}30 \text{ ml/min/1.73m}^2$, as was presented in this patient. There is currently no antidote (unlike warfarin) in the event of excessive bleeding or the need for the patient to undergo emergency surgery. There is also no long-term data on the usage of these medications as yet.

It is recommended to stop rivaroxaban at least 24 hours prior to minor surgery/mild bleeding risk and 48 hours prior to major surgery/high bleeding risk. Rivaroxaban has a

half-life of approximately 5-13 hours. Thus, stopping rivaroxaban for minor surgery will require about twice its half-life, and 4-5 times its half-life for major surgery. However, caution should be exercised for the elderly with renal impairment (eGFR <30ml/min/1.73m²). As such, rivaroxaban may need to be stopped for a longer period of time prior to surgery/intervention (Janssen Pharmaceuticals 2022).

Mastectomy is deemed high risk for developing postoperative haematoma as it involves extensive dissection leaving a large raw area. The resumption of therapeutic anticoagulants should be delayed until there is adequate healing of the wound site, with close observation of blood in the surgical drains, and dressing remaining dry, and with monitoring of the haemoglobin levels if indicated (Douketis & Lip 2019). Based on the literature, rivaroxaban may be restarted as soon as haemostasis is secured, ranging from 24-48 hours. The balance between thromboembolic and bleeding risk needs to be weighed and this will differ from case to case.

We decided to defer its commencement due to our previous experience of postmastectomy haematoma in a patient, that required surgical evacuation when she was restarted on her anticoagulant therapy 72 hours postoperatively. Hence, it is also important to take into consideration the risks of the development of a postmastectomy haematoma. as this would predispose the patient to unnecessary cardiac risks of an additional general anaesthesia. A haematoma will also increase the

risk of a surgical site infection (Song et al. 2020; Hemmingsen et al. 2022). Salemis (2017) reported a rare case of rivaroxaban-induced spontaneous chest wall expanding haematoma in a postmastectomy patient that required surgical intervention.

The right mastectomy specimen was reported to have an extensive area of intermediate grade Ductal Carcinoma In Situ (DCIS) involving the lateral half of the breast, measuring approximately 8-10 cm with clear surgical margins. The nearest was the inferior margin (1.2 cm). There were no invasive components. Both sentinel lymph nodes had no metastases (T_{is}N0M0). No adjuvant treatment was necessary for her breast malignancy, which was ER/PR negative.

CONCLUSION

In this patient with cardiopulmonary and renal dysfunction, perioperative fluid management may be guided successfully using goal directed therapy. This is important as it could ensure adequate intravascular volume to prevent both thromboembolism and cardiopulmonary complications at the same time. Restarting rivaroxaban should be delayed until there is no clinical risk of bleeding. Early commencement of oral anticoagulant therapy could potentially lead to spontaneous postmastectomy haematoma.

REFERENCES

- Al Rasyid, Harris, S., Kurniawan, M., Mesiano, T., Hidayat, R., Meisadona, G. 2019. Blood viscosity as a determining factor of ischemic

- stroke outcomes evaluated with NIHSS and MRS on Day 7 and 30 post-thrombolysis. *Int J Pharm Pharm Sci* **11**(9): 73-9.
- Angappan, S., Parida S., Vasudevan A., Badhe, A. 2005. The comparison of stroke volume variation with central venous pressure in predicting fluid responsiveness in septic patients with acute circulatory failure. *Indian J Crit Care Med* **19**(7): 394-400.
- Corcoran, T., Rhodes, J.E., Clarke, S., Myles, P.S., Ho, K.M. 2012. Perioperative fluid management strategies in major surgery: a stratified meta-analysis; *Anesth Analg* **114**(13): 640-51.
- Dardiotis, E., Aloizou, A-M., Markoula, S., Siokas, V., Tsarouhas, K., Tzanakakis, G., Libra, M., Kyritsis, A.P., Brotis, A.G., Aschner, M., Gozes, I., Bogdanos, D.P., Spandidos, D.A., Mitsias, P.D., Tsatsakis, A. 2019. Cancer-associated stroke: Pathophysiology, detection and management (Review). *Int J Oncol* **54**(3): 779-96.
- Douketis, J.D., Lip, G.Y.H. Perioperative management of patients receiving anticoagulants. 2019. <https://www.uptodate.com/contents/perioperative-management-of-patients-receiving-anticoagulants/print> [1 September 2021].
- Galie, N., Hoepfer, M.M., Humbert, M., Torbicki, A., Vachiery, J.L., Barbera, J.A., Beghetti, M., Corris, P., Gaine, S., Gibbs, J.S., Gomez-Sanchez, M.A., Jondeau, G., Klepetko, W., Opitz, C., Peacock, A., Rubin, L., Zellweger, M., Simonneau, G. 2009. Guidelines for the diagnosis and treatment of pulmonary hypertension. *Eur Respir J* **34**(6): 1219-63.
- Giglio, M.T., Marucci, M., Testini, M., Brienza, N. 2009. Goal-directed haemodynamic therapy and gastrointestinal complications in major surgery: A meta-analysis of randomized controlled trials. *Br J Anaesth* **103**(5): 637-46.
- Hemmingsen, M.N., Larsen, A., Ørholt, M., Rasmussen, L.E., Weltz, T.K., Andersen, P.S., Sarmady, F.N., Elberg, J.J., Vester-Glowinski, P.V., Herly, M. 2022. Hematoma and deep surgical site infection following primary breast augmentation: A retrospective patients. *J Plast Reconstr Aesthet Surg* **75**(3): 1197-203.
- Jansen Pharmaceuticals. <https://www.xareltohcp.com/treatment-considerations> [29 September 2021].
- Klabunde, R.E. 2022. The pharmacologic treatment of pulmonary hypertension. <https://www.cvpharmacology.com/clinical%20topics/pulmonary%20hypertension#:~:text=Normally%2C%20mean%20pulmonary%20arterial%20pressure,pressure%20is%20about%208%20mmHg.> [26 September 2021].
- Lobo, D.N., Bostock, K.A., Neal, K.R., Perkins, A.C., Rowlands, B.J., Allison, S.P. 2002. Effect of salt and water balance on recovery of gastrointestinal function after elective colonic resection: A randomised controlled trial. *Lancet* **359**(9320): 1812-8.
- Nisanevich, V., Felsenstein, I., Almogy, G., Weissman, C., Einav, S., Matot, I. 2005. Effect of intraoperative fluid management on outcome after intraabdominal surgery. *Anesthesiology* **103**(1): 25-32.
- Olesen, J.B., Torp-Pedersen, C., Hansen, M.L., Lip, G.Y. 2012. The value of the CHA₂DS₂-VASc score for refining stroke risk stratification in patients with atrial fibrillation with a CHADS₂ score 0-1: a nationwide cohort study. *Thromb Haemost* **107**(6): 1172-9.
- Pani, N., Dongare, P.A., Mishra, R.K. 2015. Reversal agents in anaesthesia and critical care. *Indian J Anaesth* **59**(10): 664-9.
- Pritts, C.D., Pearl, R.G. 2010. Anesthesia for patients with pulmonary hypertension. *Curr Opin Anaesthesiol* **23**(3): 411-6.
- Salemis, N.S. 2017. Rivaroxaban-induced chest wall spontaneous expanding hematoma. *Drug Discov Ther* **11**(1): 47-50.
- Song, J., Tark, A., Larson, E.L. 2020. The relationship between pocket hematoma and risk of wound infection among patients with a cardiovascular implantable electronic device: An integrative review. *Heart Lung* **49**(1): 92-8.
- Vincent, J.L., Pelosi, P., Pearse, R., Payen, D., Perel, A., Hoefl, A., Romagnoli, S., Ranieri, V.M., Ichai, C., Forget, P., Della Rocca, G., Rhodes, A. 2015. Perioperative cardiovascular monitoring of high-risk patients: a consensus of 12. *Crit Care* **19**(1): 224.

Received: 08 Sept 2022

Accepted: 03 Nov 2022