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EDITORIAL ARTICLE

Predictive medicine, machine learning, and anesthesia[☆]

Medicina predictiva, aprendizaje automático y anestesia

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"Whoever looks at the past, sees the future". Lope de Vega

It is easy to assume that arterial pressure (AP) contributes to perioperative morbidity and mortality. Our older colleagues will remember the need to measure AP "as you go" using sphingonometry (Korotov sounds) or simply detecting the radial pulse after deflating the cuff to obtain a systolic

In the 1990s, the introduction and widespread use of automated oscillometric AP measurement methods lightened the workload of the surgical team and allowed more frequent readings.

The anaesthesia monitoring standards published by the American Society of Anesthesiology (ASA) recommends measuring AP at least every 5 min. This recommendation is echoed by the World Health Organization (WHO) in its 2009 Safe Surgery Guidelines:2

It is evident that current anaesthesia practice involves measuring AP, among other parameters, since it is essential for good transport of oxygen and nutrients, cardiac output (flow), and also adequate perfusion pressure.

The definition of hypotension is more controversial, and a multitude of approaches are found in the literature, depend-

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ing not only on the threshold of absolute systolic, diastolic or mean AP (MAP), but also on the percentage decrease in blood pressure over baseline. Hence, according to the study by Bijker et al., the frequency of intraoperative hypotension (IOH) ranges from 5% to 99%.

From a pathophysiological point of view, MAP is the determining parameter for defining hypotension, since it represents the real pressure of blood flow. Although the threshold IOH value for the onset of tissue ischaemia will vary among individuals (age, hypertension, arteriopathy, alteration of static or dynamic autoregulation, etc.), the literature establishes a value of 60-65 mmHg.

The impact of IOH on postoperative morbidity and mortality is well defined in the literature. Salmasi et al., 4 in a cohort of 57,315 patients undergoing non-cardiac surgery, showed that the risk of acute kidney injury and myocardial ischaemia begins when MAP falls below 65 mmHg or below 20% of baseline. Another large retrospective study of 33,330 noncardiac surgery patients⁵ found similar MAP thresholds of 55 mmHg for the risk of renal failure and myocardial ischaemia. In their prospective study, Sun et al. reported identical MAP values of 55 mmHg lasting more than 20 min for renal failure, and 60 mmHg lasting 10 min for myocardial ischaemia.6

The literature not only associates IOH with kidney damage and postoperative myocardial damage, 4-11 but also establishes its association with ischaemic stroke, postoperative delirium¹²⁻¹⁴ and death. ^{10,11,15} At this point, given the incidence and consequences of IOH, we might well ask ourselves whether it can indeed be predicted.

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Machine learning is a subset of artificial intelligence that involves designing systems capable of learn automatically. The system actually consists of an algorithm in which millions of input variables or *features* are associated with other output variables, or *labels*. The computer uses this model to predict future behaviours. Machine learning is therefore used to predict a certain behaviour, and to do this it needs is to identify patterns that are undetectable to the human brain. Using thousands or millions of features and identifying their past behaviour, the computer is able to develop a predictive algorithm for the future.

Hatib et al., 16 applied machine learning to hundreds of thousands of AP waveform recordings in surgical patients or critical care units to construct a hypotension prediction index (HPI) ranging from 1 to 100. The score indicates the likelihood that a patient will have a MAP of less than 65 mmHg in the next 5-15 min, and that this MAP will last at least 1 min. The scale had a sensitivity and specificity for predicting IOH of 92% and 95% at 5 min, 89% and 90% at 10 min, and 87% and 88% at 15 min before the hypotensive event occurs. In the subsequent external validation in patients under anaesthesia, the sensitivity and specificity were 87%/89%, 84%/84% and 84%/83% at 5, 10 and 15 min, respectively. The prediction system has been commercialized, and the IOH alarm is activated when the HPI reaches a likelihood equal to or greater than 85%. This value is accompanied on the screen by other haemodynamic variables that can guide therapeutic decision according to the possible origin of IOH (contractility, preload, arterial load, vascular

In this issue, Solares¹⁷ has published a case report in which the HPI was used in a patient with dilated cardiomy-opathy who underwent liver resection. The system predicted hypotension, and allowed the surgical team to take prompt action to treat and prevent these events and identify the underlying cause.

The system has also been validated by other authors. For example, Davies et al., ¹⁸ in a retrospective analysis of 255 patients, found that the HPI system predicted hypotension with a sensitivity and specificity of 85.8% (95% CI, 85.8%–85.9%) and 85.8% (95% CI, 85.8%–85.9%) 5 min before the event occurred. ¹⁸ In another prospective, blinded, randomized study in 99 patients undergoing hip arthroplasty, Schneck et al. ¹⁹ found that HPI monitoring allowed them to significantly reduce both the absolute number of hypotensive events and their duration compared to controls.

Given that the patterns identified in the AP waveform during development of the predictive algorithm are based on the start-up of compensatory mechanisms prior to hypotension, it is logical to assume that increases in the HPI, regardless of whether or not they reach 85%, are indicative of the implementation of these mechanisms.

Although HPI is undoubtedly a promising monitoring tool, some issues still remain unresolved, for example: the extent to which morbidity and mortality are reduced by using the HPI to predict the number of hypotensive events; whether clinicians will take a more proactive attitude to treating IOH; or the potential consequences of false positives; and based on all of the above, the cost-effectiveness of the HPI system.

What is undeniable is that machine learning applied to both the clinical and technological aspects of medicine is here to stay. Liu et al., performed a meta-analysis of studies comparing the diagnostic accuracy of health-care professionals and machine learning models, and found no significant differences between the two, although they observed a tendency towards superiority in the latter. ²⁰ An investigation into the number of commercially available artificial intelligence and machine learning systems is beyond the scope of this editorial, but it is estimated that between 2 and 3 are developed each month in fields such as diagnostic imaging, oncology screening, histological diagnosis, dermatology diagnosis, etc. ²¹

Recently, Attia et al. used an artificial intelligenceenabled electrocardiogram to predict patients with left ventricular ejection fraction values of less 35% with a sensitivity and specificity of 86.3% and 85.7%, respectively.²² The same author used the same technique to identify patients with atrial fibrillation during sinus rhythm, also with high sensitivity and specificity.²³

The appearance of artificial intelligence and machine learning predictive systems in the field of anaesthesia and critical medicine is a key factor in optimising patient care, treatment and diagnosis both now and in the future.²⁴ Data from millions of electronic medical records will provide new models of care, rendering the multiple risk or prognostic scales designed so far obsolete. And an algorithm will establish the indication for surgery based on the patient's history and risk assessment, with sensitivities close to 100%. The future is now.

References

- Comitee of Origin. American Society of Anesthesiologists. Standards for Basic Anesthetic Monitoring. [Accessed 27 Feb 2020]. Available from: https://www.asahq.org/~/media/Sites/ASAHQ/Files/Public/Resources/standardsguidelines/standards-for-basic-anesthetic-monitoring.pdf.
- World Health Organization. WHO Guidelines for Safe Surgery; 2009 [Accessed 27 Feb 2020]. Available from: http://apps.who.int/iris/bitstream/10665/44185/1/97892415 98552_eng.pdf.
- 3. Bijker JB, van Klei WA, Kappen TH, van Wolfswinkel L, Moons KGM, Kalkman CJ. Incidence of intraoperative hypotension as a function of the chosen definition: literature definitions applied to a retrospective cohort using automated data collection. Anesthesiology. 2007:107:213–20.
- Salmasi V, Maheshwari K, Yang D, Mascha EJ, Singh A, Sessler DI, 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, http://dx.doi.org/10.1097/ALN.000000000001432.
- Walsh M, Kurz A, Turan A, Rodseth RN, Cywinski J, Thabane L, et al. Relationship between intraoperative mean arterial pressure and clinical outcomes after noncardiac surgery. Anesthesiology. 2013;119:507-15, http://dx.doi.org/10.1097/ALN.0b013e3182a10e26.
- Sun LY, Wijeysundera DN, Tait GA, Beattie WS. Association of intraoperative hypotension with acute kidney injury after elective noncardiac surgery. Anesthesiology. 2015;123:515–23, http://dx.doi.org/10.1097/ALN.0000000000000765.
- Bijker JB, Persoon S, Peelen L, Moons K, Kalkman C, Kappelle L, et al. Intraoperative hypotension and perioperative ischemic stroke after general surgery. Anesthesiology. 2012;116:658–64, http://dx.doi.org/10.1097/ALN.0b013e3182472320.

- Asfar P, Meziani F, Hamel J-FF, Grelon F, Megarbane B, Anguel N, et al. High versus low blood-pressure target in patients with septic shock. N Engl J Med. 2014;370:1583–93, http://dx.doi.org/10.1056/NEJMoa1312173.
- Devereaux PJ, Yang H, Yusuf S, Guyatt G, Leslie K, Villar JC, et al. Effects of extended-release metoprolol succinate in patients undergoing non-cardiac surgery (POISE trial): a randomised controlled trial. Lancet. 2008;371:1839–47, http://dx.doi.org/10.1016/S0140-6736(08)60601-7.
- 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, http://dx.doi.org/10.1097/ALN.0000000000000686.
- 11. Monk TG, Bronsert MR, Henderson WG, Mangione MP, Sum-Ping STJ, Bentt DR, et al. Association between intraoperative hypotension and hypertension and 30-day postoperative mortality in noncardiac surgery. Anesthesiology. 2015;123:307-19, http://dx.doi.org/10.1097/ALN.0000000000000756.
- Tognoni P, Simonato A, Robutti N, Pisani M, Cataldi A, Monacelli F, et al. Preoperative risk factors for postoperative delirium (POD) after urological surgery in the elderly. Arch Gerontol Geriatr. 2011;52:e166-169, http://dx.doi.org/10.1016/j.archger.2010.10.021.
- Hirsch J, DePalma G, Tsai TT, Sands LP, Leung JM. Impact of intraoperative hypotension and blood pressure fluctuations on early postoperative delirium after non-cardiac surgery. Br J Anaesth. 2015;115:418–26, http://dx.doi.org/10.1093/bja/aeu458.
- **14.** Aldemir M, Ozen S, Kara IH, Sir A, Baç B. Predisposing factors for delirium in the surgical intensive care unit. Crit Care. 2001:5:265-70.
- 15. Willingham MD, Karren E, Shanks AM, O'Connor MF, Jacobsohn E, Kheterpal S, et al. Concurrence of intraoperative hypotension, low mini-mum alveolar concentration, and low bispectral index is associated with post-operative death. Anesthesiology. 2015;123:775–85, http://dx.doi.org/10.1097/ALN.0000000000000822.

- Hatib F, Jian Z, Buddi S, Lee C, Settels J, Sibert K, et al. Machine-learning algorithm to predict hypotension based on high-fidelity arterial pressure waveform analysis. Anesthesiology. 2018;129:663–74.
- 17. Solares G, Barredo F, Monge García I. El valor del Índice de Predicción de la Hipotensión y el dP/dt_{max} para predecir y tartar la hipotensión en un paciente con una miocardiopatía Dilatada. Res Esp Anestesiol Reanim. 2020.
- Davies SJ, Vistisen ST, Jian Z, Hatib F, Scheeren TWL. Ability of an arterial waveform analysis-derived hypotension prediction index to predict future hypotensive events in surgical patients. Anesth Analg. 2020;130:352-9, http://dx.doi.org/10.1213/ANE.0000000000004121.
- Schneck E, Schulte D, Habig L, Ruhrmann S, Edinger F, Markmann M, et al. Hypotension Prediction Index based protocolized haemodynamic management reduces the incidence and duration of intraoperative hypotension in primary total hip arthroplasty: a single centre feasibility randomised blinded prospective interventional trial. J Clin Monit Comput. 2019, http://dx.doi.org/10.1007/s10877-019-00433-6.
- 20. Liu X, Faes L, Kale AU, Wagner SK, Fu DJ, Bruynseels A, et al. A comparison of deep learning performance against health-care professionals in detecting diseases from medical imaging: a systematic review and meta-analysis. Lancet Digital Health. 2019;1:e271-97.
- 21. Rajkomar A, Dean J, Kohane I. Machine learning in medicine. N Enl J Med. 2019;380:1347–58.
- 22. Attia ZI, Kapa S, Lopez-Jimenez F, McKie PM, Ladewig DJ, Satam G, et al. Screening for cardiac contractile dysfunction using an artificial intelligence-enabled electrocardiogram. Nat Med. 2019:25:70–4.
- 23. Attia ZI, Noseworthy PA, Lopez-Jimenez F, Asirvatham SJ, Deshmukh AJ, Gersh BJ, et al. An artificial intelligence-enabled ECG algorithm for the identification of patients with atrial fibrillation during sinus rhythm: a retrospective analysis of outcome prediction. Lancet. 2019;7:861–7, 394.
- Hashimoto DA, Witkowski E, Gao L, Meireles O, Rosman G. Artificial intelligence in anesthesiology: current techniques, clinical applications, and limitations. Anesthesiology. 2020;32:379–94.