Nomogram to estimate age-related MAC

J. G. C. Lerou*

Radboud University Nijmegen, Department of Anaesthesia, Geert Grooteplein 10, 6500 HB Nijmegen, The Netherlands

*E-mail: j.lerou@anes.umcn.nl

Background. In clinical practice it is difficult to estimate rapidly two important values: (i) the total age-corrected MAC multiple from measured end-expired concentrations of volatile agent and nitrous oxide; (ii) the end-expired concentration of volatile agent needed to obtain a given total MAC multiple. We have developed a nomogram to do this.

Methods. We used standard nomogram methods to construct one single nomogram covering wide ranges of age (1–100 yr) and MAC (0.1–1.8 MAC) for halothane, enflurane, isoflurane, sevoflurane, and desflurane, alone or in combination with various concentrations of nitrous oxide. The user only has to draw two straight lines to obtain the desired result.

Results. The nomogram is simple to use. End-expired concentrations of halothane 0.48%, enflurane 1.05%, isoflurane 0.75%, sevoflurane 1.18%, or desflurane 4.3% in the presence of nitrous oxide 50% will give 1.4 MAC in a patient of 75 yr whereas 0.9 MAC in a 1-yr-old. A reverse example is: a total MAC of 1.3 when using sevoflurane and nitrous oxide 67% in oxygen, requires an end-expired sevoflurane concentration of 1.8% in a 3-yr-old whereas 0.55% is needed in a patient of 90 yr.

Conclusions. The nomogram gives accurate results if it covers a whole A4 sheet in landscape format and could be extended to apply to other agents, for example xenon.

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MAC, the minimum alveolar concentration at 1 atm that prevents movement in 50% of patients exposed to surgical incision, is well established as a measure of anaesthetic potency. MAC decreases with increasing age. MAC for a given age (MAC\text{age}) can be represented as a function of MAC at 40 yr (MAC\text{40}):\(^{1}\)

\[
\text{MAC}_{\text{age}} = \text{MAC}_{\text{40}} \times 10^{-0.00269(\text{age} - 40)}. \quad (1)
\]

The end-expired concentration (\(F_E\)) of any one agent \(i\) can be expressed as a multiple (or submultiple) \(k_i\) of the relevant value of MAC:\(^2\)

\[
\frac{F_E,i}{\text{MAC}_{\text{age},i}} = k_i \quad (2)
\]

The total MAC multiple of a volatile anaesthetic agent given with nitrous oxide in oxygen is:\(^2\)

\[
k_{\text{total}} = k_{\text{volatile}} + k_{\text{N}_2\text{O}}. \quad (3)
\]

Combining equations (1), (2), and (3), yields the total age-related MAC expressed in MAC units:

\[
k_{\text{MAC},i} = \frac{F_E,i}{\text{MAC}_{\text{40},i} \times 10^{-0.00269(\text{age} - 40)}}
\]

\[
k_{\text{MAC},i} = \frac{F_E,N_2O}{\text{MAC}_{\text{40},N_2O} \times 10^{-0.00269(\text{age} - 40)}} \quad (4)
\]

Applying equation (4) is difficult in the clinical setting. Recently, Nickalls and Mapleson\(^2\) reported a graphical solution to remove this difficulty. They developed three different Cartesian charts for the 0.6–1.6 MAC range and age range 5–95 yr, that is one chart for each of the inhalation anaesthetics isoflurane, sevoflurane, and desflurane given alone or with nitrous oxide 50 or 67%.

We set out to develop one single nomogram for a wider range of MAC (0.1–1.8 MAC) and age (1–100 yr), suitable not only for isoflurane, sevoflurane, and desflurane, but also for halothane and enflurane, alone or in combination with various concentrations of nitrous oxide.
Methods and results

Equation (4) can be used for a patient of a given age in two clinically important ways: (i) to estimate the total MAC multiple from the measured end-expired concentrations of volatile agent and nitrous oxide; (ii) to find the end-expired concentration of volatile agent needed for a given total MAC multiple in the absence or presence of a given end-expired concentration of nitrous oxide. Using methods described by Levens, we developed a nomogram (Fig. 1) for the relations between the variables in equation (4) in three steps.

Step 1. If we let \( g = \frac{10^{-0.00269 \times (\text{age} - 40)}}{C_0^{0.00269}} \) and MAC\(_{40}\) for nitrous oxide = 104%, algebraic manipulation reduces equation (4) to:

\[
g k_{\text{total}} = F_{E, \text{volatile}} \frac{1}{\text{MAC}_{40, \text{volatile}}} + F_{E, N_2O} \frac{104}{104}
\]

Equation (5) is in a type form known in nomography: \( q = u \cdot v + t \), where \( q = g k_{\text{total}} \) and \( t \) is a constant for a given value of the end-expired concentration of nitrous oxide. The latter two equations may be represented by a combination of two alignment charts with a common axis for \( q \) (turning axis).

Step 2. A ‘Z-chart’ is constructed for the relation \( q = u \cdot v + t \), where \( q = g k_{\text{total}} \) and \( t \) is a constant for a given value of the end-expired concentration of nitrous oxide. The latter two equations may be represented by a combination of two alignment charts with a common axis for \( q \) (turning axis).

Step 3. A ‘net chart’ is constructed for the relation \( q = u \cdot v + t \). The net chart consists of superimposed Z-charts. There is one Z-chart for the relation (\( q = u \cdot v \)) per value of \( t \), that is per value chosen for the end-expired concentration of nitrous oxide. The end-expired concentration for the volatile agent and \( q \) are on the parallel scales, MAC\(_{40, \text{volatile}}\) is on the diagonal scale. The parallel scales are the same for each value of \( t \), but there is one diagonal scale for each value of \( t \).

Mathcad 2000 (Mathsoft Europe, UK) was used for the mathematics, and Axum 6 (Mathsoft) and Visio 2000 (Microsoft) for the graphics. The mathematics in the Mathcad worksheet can be easily tailored to other intervals of interest, for example for \( k_{\text{total}}, \text{MAC}_{40}\) for halothane, isoflurane, enflurane, sevoflurane, and desflurane was 0.75, 1.17, 1.63, 1.80, and 6.60%, respectively. Because of the wide ranges in MAC\(_{40}\) and \( k_{\text{total}} \), we graduated the end-expired concentration axis on both sides (Fig. 1). The range is 0–4.13% (=1.8 MAC sevoflurane in a 1-yr-old) for all agents but desflurane. Desflurane uses a 5-fold larger range. This approach increased accuracy.

The nomogram is used as follows (Fig. 1). Consider a 3-yr-old for whom the measured end-expired concentrations of forming a ‘Z’. A straight line joining values on two of the scales will intersect the third scale at a value that satisfies the relation between the variables, that is one is the product of the other two. Age and \( q \) are on the parallel scales and \( k_{\text{total}} \) is on the diagonal scale.

Fig 1 Nomogram relating age, total MAC expressed in MAC units, and end-expired concentrations of volatile agent and nitrous oxide. A result is found by drawing two straight lines. Example (dotted lines): if the measured end-expired concentrations of sevoflurane and nitrous oxide are 1.8 and 67% (at 1 atm), respectively, then the total age-related MAC is 1.3 in a 3-yr-old. Reverse example: a total MAC of 1.3 in a 3-yr-old, when using sevoflurane and nitrous oxide 67% in oxygen, requires an end-expired sevoflurane concentration of 1.8%. See text for details and the Appendix for adding extra volatile agents and other concentrations of nitrous oxide or xenon.
sevoflurane and nitrous oxide are 1.8 and 67%, respectively. To find the total age-related MAC, first draw a straight line joining the point 1.8% on the end-expired concentration axis and the symbol corresponding to the use of sevoflurane in oxygen/nitrous oxide 67%. The intersection of this line with the turning axis is then joined with the point 3 yr on the age axis. The intersection with the total MAC axis yields 1.3 MAC. Applying equation (4) would yield 1.31 MAC.

The nomogram can be used in reverse. Suppose it is required to achieve 0.6 MAC in a 90-yr-old using isoflurane in oxygen/air. First draw a straight line through the positions for age 90 and total MAC 0.6. The point where this line cuts the turning axis is joined with the symbol corresponding to the use of isoflurane alone. Intersection with the axis for the end-expired concentrations yields 0.52%.

Comment
We found the nomogram to be simple to use clinically, yielding very accurate results if it covers a whole A4 sheet in landscape format.

The wide 0.1–1.8 MAC range of the nomogram enhances its usefulness by including variants of MAC.5 MAC-awake (MACaw), the end-expired concentration at 1 atm suppressing appropriate response to command in 50% of patients, is one-third of MAC for isoflurane, sevoflurane, or desflurane, but 0.55 MAC for halothane.5 MACaw decreases with age at the same rate as does MAC. Memory is also lost at MACaw. The sub-1 MAC range can be used to supplement remifentanil infusions because MAC and its other variant MACbar are decreased by opiates.7 MACbar is the alveolar concentration which blocks adrenergic responses (increases in heart rate and arterial pressure) to skin incision. MACbar for halothane, isoflurane, or desflurane is 1.3–1.5 MAC, but for sevoflurane 3.5 MAC has been reported.4

As defined effects of volatile anaesthetic agents correlate well with their end-expired partial pressures, use of the nomogram in conjunction with a reliable gas analyser is clinically meaningful. Also, when combining inhaled anaesthetics, there is evidence to support an additive effect1,2,5 (and references therein). Therefore, to paraphrase White,4 it would be possible to argue that knowledge of ktotal is at least as good as a guide to the presence or absence of the anaesthetic state as other methods of measuring depth of anaesthesia when allowing for the lag between end-expired and brain concentrations (compare with Figs 5 and 6 in ref.8).

Use of the nomogram must be based, however, upon sound clinical judgement and careful interpretation of available data. The crucial assumption of additivity of effects may not be totally correct. Published data suggest that the MAC-reducing effect of nitrous oxide in children is attenuated in the presence of less soluble volatile agents9 (and references therein). In 1–3-yr-old patients nitrous oxide 60% decreased the MAC of sevoflurane by only 24%, which is less than half the expected value.9 Although the nomogram corrects for age, it does not allow for all biological variability in MAC as described by Sonner.10 Thus, it may be useful to estimate not only ktotal but also ktotal=20%. The MAC40’s used are for patients at 37°C, but MAC decreases with decreasing body temperature, at least in animals.5

Some elements were omitted from the nomogram for the sake of clarity. The turning axis has no graduations because these would show only the clinically unimportant values for q. The three diagonal lines representing the MAC40 scales for 0, 50, and 67% nitrous oxide were not drawn because the symbols suffice. As MAC40 for xenon=72%, the diagonal scales for nitrous oxide 50 or 67% can be used for xenon 35 or 46%, respectively. The appendix shows how to add other concentrations and extra volatile agents.

Using the new nomogram an anaesthetist can rapidly determine the depth of anaesthesia in age-corrected MAC units for each of the five youngest volatile anaesthetics, even when administered with nitrous oxide.

Appendix
The theory behind the nomogram explaining how the axes are positioned and calibrated is treated in textbooks such as the one used3 or those referenced therein and on http://www.ece.rochester.edu/~jones/NomoDevel/nomoRef.htm. Nevertheless, extra volatile agents or other concentrations of nitrous oxide or xenon may be added to the nomogram in its present form.

Step 1. In the absence of nitrous oxide or xenon the diagonal scale is the line joining zero on the axis for the end-expired concentration (point O1) and zero on the turning axis (point O2, where the turning axis intersects the total MAC axis). If L is the full length of this line, an extra symbol is situated at a distance L/[1+(a/MACaw,volatile)] from O1, where q=9 or q=1.8 (left or right graduations being used on the end-expired concentration axis, respectively).

Step 2. For each concentration of nitrous oxide or xenon a diagonal scale is ruled from O1 to a point on the turning axis at a distance HF,//b from point O2. H is the length of the turning axis, and b=238.4 for i=nitrous oxide or b=165.0 for i=xenon.

Step 3. The symbols for one volatile agent but different concentrations of nitrous oxide or xenon are on a vertical line through the symbol found in step 1 (Fig. 1).

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