



AUDIT, RESEARCH AND GUIDELINE UPDATE

The 'anatomic shunt test' in clinical practice; contemporary description of test and in-service evaluation

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ABSTRACT

The 100% oxygen shunt test for detecting right-to-left anatomical shunting was originally described 70 years ago. However, its clinical value is not yet established. We conducted an audit in 80 patients undergoing the test between 1996 and 2012 in a tertiary referral centre. A significant difference ($p=0.02$) existed between the median shunt percentages where anatomical shunting was identified (10.2%) and absent (5.0%). The area under the curve for a ROC plot was 0.70. A shunt percentage of 8.3 had a sensitivity of 80% and specificity of 75% for detection of an anatomic shunt. We conclude the test is satisfactory for the first-line investigation for anatomic shunting.

INTRODUCTION

A rare but important cause of arterial hypoxaemia is the anatomical right-to-left shunting of blood past ventilated alveoli. The normal shunt fraction of 5% of cardiac output can pathologically increase in congenital heart disease, pulmonary arteriovenous malformations (PAVM) and hepatopulmonary syndromes.

The detection of right-to-left anatomical shunting is not always clinically straightforward. One non-invasive method is the classical 100% oxygen shunt test that can be readily performed in most pulmonary function departments. The technique described more than 70 years ago¹ relies on rebreathing 100% oxygen and measurement of the resulting pO_2 . A shunt fraction of greater than 5% is said to indicate a high likelihood of an anatomical shunt.

Although descriptions of the shunt test in hereditary haemorrhagic telangiectasia exist, the clinical value of the test in the broader context of respiratory medicine is not well established, nor is it known what magnitude of shunt may be considered abnormal.

We performed an audit of patients undergoing anatomical shunt studies between April 1996 and November 2012 in a tertiary referral centre. We also provide a fuller description of the 100% oxygen shunt test since Berggren's original description is not readily available.¹

100% OXYGEN SHUNT TEST

Knowing FiO_2 , barometric pressure and $PaCO_2$, it is possible to calculate the ideal pO_2 that may be achieved using the following formula:

$$(P_{BAR} - 6.27 \times FiO_2) - PaCO_2$$

A blood gas measurement from the radial artery with the patient breathing room air is performed to measure $PaCO_2$. The patient is seated with a nose clip and allowed to breathe for a minimum of 20 min from a 200 L Douglas bag filled with 100% oxygen.

End tidal oxygen values were monitored with a respiratory mass spectrometer. Stable oxygen end tidal values are indicative of equilibration and complete washout with 100% oxygen, at which time a second radial artery blood gas sample is taken and analysed immediately.

The shunt fraction is then calculated from the following equation:

$$\% \text{Cardiac Output} = \frac{\text{Ideal } PaO_2 - \text{Actual } PaO_2}{2.66}$$

The methodology assumes that after breathing 100% oxygen until equilibrium, nitrogen washout from poorly ventilated areas will eliminate any V_A/Q mismatching, and thus, that any reduction in the 'ideal' PaO_2 is due to shunting. Of note, below a PaO_2 of 13.33 kPa the relationship between arterial oxygen content and partial pressure is no longer linear due to the shape of the oxygen-haemoglobin dissociation curve. Therefore, using this formula a maximum shunt of only 30% can be measured.

METHODS

In total, 189 patients between April 1996 and November 2012 underwent the shunt test. Eighty-one sets of clinical notes were available for review and were subsequently included. There was no significant difference in age ($p=0.81$), gender ($p=0.55$) or shunt fraction ($p=0.10$) between the group included and the group not included. One patient was excluded from subsequent analysis as he had an established diagnosis of an existing anatomical shunt that was being quantitatively assessed. This was a retrospective audit and in-service evaluation for which our local ethical committee has ruled that permission is not required.

RESULTS

Eighty patients who underwent the shunt test were included in the case review; 51% were men, the mean age was 50.2 years and 24% of patients underwent the test as an inpatient. The main



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indication for the test was disproportionate hypoxia given the underlying disease (61%) followed by symptomatic shortness of breath (21%). Within a 6-month period of a patient undergoing the 100% oxygen testing, additional tests undertaken were as follows: contrast echocardiography (39%), transthoracic echocardiography (39%), cardiac catheterisation (20%), ^{99m}Tc -labelled albumin aggregated scan (8%), CT (45%) of which 10% were CT pulmonary angiograms. Thirteen patients (16%) with a low clinical probability of having a shunt did not undergo any further investigations after having an initial 100% oxygen test, and subsequently their data were not included in the shunt analyses.

A clinical conclusion of an anatomical shunt was based on either positive contrast echocardiography (grade I or above) and/or a positive catheter study with the identification of a cardiac or a pulmonary shunt. A significant difference ($p=0.02$) existed in the median shunt percentage obtained from the 100% oxygen test between patients with an identified anatomical shunt (10.2%) and in those without (5.0%). Age ($p=0.48$), gender ($p=0.15$) or resting PaO_2 on air ($p=0.22$) were not different between positive and negative cases. There was no significant difference in the shunt values in patients with or without an underlying lung disease ($p=0.66$).

In total, 15 patients (18.8%) had an anatomical shunt identified. Eleven of these patients had established underlying lung disease; however, this was not significant ($p=0.76$). Six patients (40%) subsequently underwent interventions to correct the shunting.

A receiver–operator characteristic (ROC) curve was derived (figure 1). The area under the curve was 0.70 ($p=0.02$) and the inflection existed at 8.3%, with a sensitivity of 80% and specificity of 75%. At 5% cut-off, the sensitivity of the test for an identifiable shunt was 80% and specificity 50%. Of the 13 patients excluded due to not having other tests performed, all had shunt values below 8.3% and 10/13 had a shunt value of 5% or below. Including these patients in the analyses did not change the inflection point.

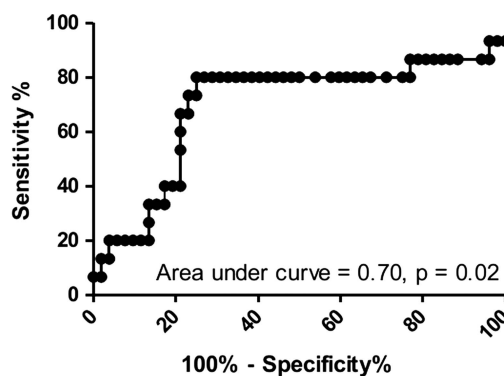
DISCUSSION

In this paper, we provide a description of the contemporary practice of the 100% oxygen test that has hitherto been well characterised only for PAVM screening in the context of hereditary haemorrhagic telangiectasia. Although the value of the test is context-dependent, we found that a calculated shunt of more than 8.3% has a sensitivity of 80% and specificity of 75% for the presence of an anatomically defined shunt. This value is similar to a prospective study of 111 patients undergoing screening for PAVMs in the context of possible hereditary haemorrhagic telangiectasia with chest CT as the gold standard.²

As with any physiological test, care must be taken with both the technique and equipment to reduce risk of inaccuracies. Assumptions on cardiac output, haemoglobin concentration and oxygen consumption values are made. Additionally, it has been suggested that breathing 100% oxygen could encourage alveolar collapse as the alveolar-splinting effect of poorly soluble nitrogen is lost.

The relationship between anatomical shunting and inspired oxygen is complex. The potential to lower pulmonary artery pressure by inhalation of high fractional concentrations of oxygen may allow temporary closure of an existing patent foramen ovale and reduce measured shunting.³ Furthermore, alteration of pulmonary pathways with the variation of inspired oxygen concentration is hypothesised to occur. Volunteers subjected to hypoxia ($\text{FiO}_2=0.12$) or exercise developed new intrapulmonary shunting when measured through contrast echocardiography,⁴ while hyperoxia ($\text{FiO}_2=1.0$) prevented exercise-induced shunting. This potential modulation on anatomical pathways may affect accuracy in the measurement of shunting through the oxygen shunt test.

Contrast echocardiography remained positive in 90% of patients who underwent successful transcatheter embolisation. However, in the same cohort, the oxygen shunt test normalised in 73% of patients postembolisation. In this context, discordance between the tests may occur because of the existence of microscopic arteriovenous communications undetectable by CT or angiography.⁵



Cut-off for abnormal shunt fractions (%)	Sensitivity (%)	95% Confidence Interval (%)	Specificity (%)	95% Confidence Interval (%)	Likelihood ratio
> 2.2	86.7	59.5 to 98.3	11.5	4.4 to 23.4	1.0
> 4.0	80.0	51.9 to 95.7	34.6	22.0 to 49.1	1.2
> 5.0	80.0	51.9 to 95.7	50.0	35.8 to 64.2	1.6
> 6.1	80.0	51.9 to 95.7	57.7	43.2 to 71.3	1.9
> 8.3	80.0	51.9 to 95.7	75.0	61.1 to 86.0	3.2
> 10.3	40.0	16.3 to 67.7	78.9	65.3 to 89.0	1.9

Figure 1 Receiver–operator characteristic plot and table of values in the oxygen shunt test ($n=67$).

CRITIQUE OF THE METHOD

Our data would have been stronger if we had collected them prospectively with the protocolised collection of phenotypic data; however, the 100% oxygen test is seldom performed even in an institution with a national referral base and no such data exist despite 70 years elapsing since Berggren's original description. Nevertheless, the test is fundamentally straightforward and in principle can be performed anywhere that arterial blood gases and carbon dioxide can be measured.

The value of any test depends heavily on the pretest probability of a positive result, and the present data will be translatable to institutions with a similar caseload. In that context, we emphasise that the majority of shunt tests were performed because of an unexplained hypoxia (61%). There exists a significant difference (10.2% vs 5.0%; $p=0.02$) in the shunt fraction between positive and negative cases of anatomical shunting using the 100% oxygen test.

A further limitation to our case review is the lack of a gold standard test available for the identification of anatomic shunting. Despite this, based on the methodology that we have applied in this report, we conclude that 8.3% is a more appropriate cut-off for the 100% oxygen test providing improved specificity than 5%.

The 100% oxygen shunt test is a safe and non-invasive test that allows quantification of the shunt fraction that can be undertaken in any hospital. As a first-line screening test in a tertiary institution, we found that it has a satisfactory sensitivity and specificity for anatomically detectable shunts. We suggest a

value $>8.3\%$ be used to determine, in conjunction with other data, whether more invasive tests are desirable in the management of unexplained hypoxia.

Contributors DM collected and analysed the data, and wrote the initial draft of the manuscript. MIP designed the data collection and is the corresponding author. MSP was involved in statistical analysis. SW provided the oxygen protocol used and references involved. NSH was involved in provision of the anatomical shunt data used in the case series. All authors contributed to the redrafting and approval of the submitted manuscript.

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Competing interests None.

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