# A Short History of Provocative Maneuvers During tcpO2 Testing

Following two decades of almost exclusive use in the neonatal setting, transcutaneous oxygen tension ($tcpO_2$) screening was briefly studied as a means to predict skin flap survival on the strength of changes in flap oxygen tension, beginning in 1979.[1] This cited paper also included the first reported use of a provocative maneuver, namely 100% oxygen inhalation, during the testing process. TcpO2 evaluations were subsequently and more robustly studied within the vascular surgery discipline, beginning in the mid 1980's. [2,3,4,5] Here, they were considered to represent a more effective assessment of lower extremity arterial perfusion than standard hemodynamic and anatomic measures. This collective opinion was based upon an emerging appreciation that PVD patient disability and risk of developing complications was more a consequence of inadequate oxygenation than insufficient blood pressure, *per se*. In this setting, $tcpO_2$ testing was recognized to specifically measure degree of tissue oxygen delivery. Air breathing values alone, however, were unable to establish a diagnosis of PVD, i.e. were low values a function of local micro vascular impairment, or regional large vessel disease, or perhaps a combination of these two factors?

It was also apparent that testing under air breathing only conditions failed to discriminate peripheral vascular disease from systemic oxygenation shortcomings; were low extremity values the consequence of regional arterial occlusive disease or a central cardiopulmonary insufficiency? Or, were they entirely the result of localized small vessel pathology, something apparently not considered or at least not referenced, in these early publications. Any such discrimination was not simply a matter of academic interest. The clinical basis for this particular non-invasive vascular assessment at this time was an attempt to non-invasively determine anatomic distribution of any existing PVD in order to guide surgical planning.

To aid in differentiation of peripheral vs. systemic disease then, several provocative maneuvers were trialed. One or more might serve to assess regional vascular capacity in response to various 'stress' induced situations. The first maneuver introduced within the vascular discipline was treadmill exercise.[6] Real time observations detected decreased extremity oxygenation (defined as a falling regional perfusion index; RPI representing the ratio of extremity to chest oxygenation, expressed as a decimal) in those with complaints consistent with PVD. Such falls were not observed in healthy subjects or those who had undergone successful lower extremity flow augmentation. The problem with treadmill exercise, however, was that it was poorly suited in those with amputations, and poorly tolerated in those who were suffering rest pain or claudication, and those with lower extremity ulcerations.

The next attempt at a provocative maneuver, one that largely avoided the above shortcomings, was the introduction of temporary limb ischemia.[7] Ischemia was achieved with a pneumatic blood pressure cuff inflated below the knee. Following sensor calibration and air breathing 'pre-occlusion' determinations of tissue oxygen at the mid-calf and dorsum of the foot, the cuff was inflated to 50 mmHg above systolic arterial pressure and held for four minutes. Upon cuff release, time to 50% recovery of 'baseline' $tcpO_2$

(termed **T**ranscutaneous **O**xygen **R**ecovery **T**ime, or TORT) was recorded. Normal subjects had a TORT of less than 1.5 minutes. PVD patients had significantly longer ($p < 0.001$) TORT times, frequently ranging from 2.5 – 4.5 minutes. In some with PVD, TORT never achieved pre-occlusion testing values during the observation period, while normal limbs generally did.

TORT, while considered to identify presence of PVD, was not specific enough to determine its degree. It was also problematic to some patients, where prolonged periods of arterial compression were uncomfortable and poorly tolerated, particularly in those with pre-existing rest pain or claudication. Concern was also expressed regarding potential adverse effects of this period of compression on calcified vessels, where plaque might become dislodged, migrate arterially and occlude the distal microvasculature. Within a decade its use as a provocative maneuver had all but been discontinued.

Next up in the evolution of extremity provocative maneuvers during tcpO2 testing was 'positional change'.[8] This process involved a 45° limb elevation in the supine patient. Values obtained during extremity elevation were compared to those while standing and while supine. Importantly, analysis was based on computed change in regional perfusion index (as noted previously, RPI represents the extremity to chest oxygen ratio). As a provocative maneuver, limb elevation-induced changes in RPI overcame problems and concerns associated with both previous measures. In the context of this particular determination of PVD, it is important to emphasize that limb elevation was never meant to be a stand-alone assessment of lower extremity arterial perfusion, *per se*. Rather, it served as a simple and reproducible method to 'stress' the RPI. Further, published data involved patients positioned supine, rather than the semi-recumbent position employed by many who continue to use this maneuver today. The limb would be elevated until tcpO2 values stabilized. There was no fixed elevation time, rather it was a patient-specific period.

Resulting changes in RPI were used to diagnose existence of PVD and guide arterial flow augmentation decision-making. This particular maneuver also had the advantage of being able to serially follow patients with non-severe PVD, as determined by any changes in RPI over time. Importantly, limb elevation's effect on RPI did not assess for the presence and quality of established collateral vessels in the setting of significant PVD, nor was it able to assess presence of distal micro vascular disease.

Limb elevation-induced RPI changes thus became a commonly employed provocative maneuver. It was never, however, intended to assess perfusion in the distal lower extremity in the setting of a problem wound cases.

During this same period tcpO2 testing was increasingly employed as a method to determine optimal lower extremity amputation site. [9, 10]

By the late 1980's, and following several years of limited clinical experience, $tcpO_2$ testing began its selective employment in the practice of hyperbaric medicine. In those with lower extremity wound healing deficiencies it was used to determine if such deficiencies were hypo-perfusion/hypoxia mediated, thereby suggesting a basis for provision of oxygen supplementation.


Initial screening of hyperbaric referrals was confounded by a lack of guidance as to how best to conduct a test; namely, where exactly to place the electrode(s), single versus multiple data collection sites, preferred provocative maneuver, and what other potentially useful information could be acquired.

The first hyperbaric-specific tcpO2 studies were conducted by USAF investigators.[11] They had sought to determine if hyperbaric oxygen exposures elevated peri-wound oxygen levels, and were eventually able to confirm that this did indeed occur. Further, they were able to demonstrate that serial peri-wound 1 ATA air breathing tcpO2 values increased over a course of HBO therapy in those whose wounds that went on to heal, while they did not in non-responders. This concept of improvement in peri-wound tissue oxygenation over time as an indicator of therapeutic response remains an important but underappreciated determinant today.

At hyperbaric meetings during the mid to late 1980's frustration was frequently expressed regarding the utility of tcpO2 testing. Commonly, the complaint was that wound hypoxia had been demonstrated yet a course of HBO therapy had failed to result in healing. Conversely, others would note values that were essentially normal and their wounds did not heal? Why one would consider HBO therapy in a normally oxygenated wound was not reconciled. No effort appeared to have been made to determine whether findings of hypoxia were locally, regionally or systemically mediated, and whether or not any such wound site hypoxia was reversible (another key to the use of HBO therapy in deficient wound healing). Obviously, in wounds with a hypoxic underpinning, patients must possess the physiologic capacity to respond locally to elevated oxygen pressures delivered systemically. Because the concept of the comprehensive wound healing center had not yet been conceived, it was also likely that many such hyperbaric referrals had not been adequately worked up for deficient healing etiologies other than local hypoxia, conditions for which HBO therapy would not be expected to therapeutically impact.

During this same period, limb elevation change in RPI index remained the prevailing provocative maneuver within the vascular surgery service. However, such a maneuver was not able to address the required perfusion-related questions in order to guide hyperbaric medicine decision-making. Limb elevation-induced changes in RPI merely indicated presence of PVD. Instead of determining how much a tcpO2 value might fall, one needs to determine how much of an increase in local oxygen delivery can be achieved during oxygen inhalation. Briskly reversible peri-wound hypoxia is the basis for the use of HBO therapy. If existing hypoxia was indeed reversible then the physiologic capacity to respond locally (the wound) to centrally-delivered (lung) hyperbaric oxygenation had been demonstrated. So, adequacy of both central *and* peripheral vascular health is required if patients are to be expected to gain any benefit from HBO therapy.

100% oxygen inhalation as a provocative maneuver offers several distinct advantages to the hyperbaric medicine problem wound referral. It directly assesses and verifies the basis for HBO therapy, in that therapeutic increases in oxygen can be delivered to locally hypoxic tissues. Again, with 100% oxygen

administration as a provocative maneuver one is measuring a patient's ability to increase oxygen delivery at the wound site, rather than identifying limitations in regional arterial blood flow. Another

important and unique advantage of 100% oxygen is that it lends itself to in-chamber treatment pressure optimization. Admittedly, the present data only allows a determination of a transcutaneous oxygen tension that should be exceeded in order to minimize likelihood of treatment failure [12] rather than the optimal hyperbaric oxygen dose to promote effective wound healing.

For the wound healing deficient patient referred to the hyperbaric medicine service, therefore, oxygen inhalation is the only provocative maneuver that is able to adequately determine each of the answers sought. This 'oxygen challenge' assesses the physiologic capacity to respond, or otherwise, at the hypoxic wound margin to increases in centrally delivered oxygen. While the patient is in the hyperbaric chamber it is used to confirm the likelihood that a therapeutic dose is being achieved. [12]

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