A Clinical Evaluation of Contemporary Oxygenators: A Multi Centre Evaluation

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Abstract: There have been a number of advancements in cardiopulmonary bypass equipment with the goal of improving outcomes for cardiac surgery patients including enhancements to the oxygenator. To date, there are few clinical evaluations of contemporary oxygenators and all are single-center experiences. Methods: The current manuscript is a multicenter quality assurance evaluation of contemporary oxygenators (LivaNova Inspire 8F, Maquet Quadrox-i and Terumo FX25) and evaluated *key* metrics including gas exchange, pressure gradients and effects on patient hematology during CPB from two hospitals and compared to findings of a recently published manuscript. Results: There was heterogeneity in gas exchange both between different oxygenators and the *same* oxygenator at *different* centers, specifically the LivaNova Inspire 8F had the lowest O_2 transfer among oxygenators evaluated and the LivaNova Inspire 8F at one center had lower O_2 transfer than the other center. While there were no differences between sweep gas flow rate required to obtain a $PaCO_2$ of 40 mmHg between oxygenators, one center using LivaNova Inspire 8F required less sweep gas flow rate than the other to achieve this value. Pressure gradients varied among oxygenators with Maquet Quadrox-i having the lowest gradient pre to post oxygenator. The LivaNova Inspire 8F oxygenator had the largest drop in hemoglobin, while Terumo FX25 had the greatest platelet retention. Despite equivalency between oxygenators in terms of white blood cell proliferation, there was heterogeneity between Terumo FX25 used at two centers. In terms of neutrophils specifically, the Maquet Quadrox-i had the lowest levels, while Terumo FX25 at one site was greater than that at the other site. Conclusion: These observed differences support the need for perfusion departments to conduct their own quality assurance evaluations in order to better understand the care they are providing their patients with ongoing goal of optimizing perfusion care.

Introduction:

Along with advancements in cardiac surgery and anesthetic practices, advancements in perfusion practices and equipment have focused on improved patient safety. The piece of cardiopulmonary bypass (CPB) equipment that received the greatest attention is the oxygenator (1), which has been engineered to have reduced priming volumes, improved gas exchange, heat transfer and improved gaseous emboli (macro and micro) handling with the goal of improving patient outcomes (2,3).

Oxygenator performance parameters are readily available from manufacturers and all exceed minimal standards (4,5,6). Unfortunately, clinical evaluations of contemporary oxygenators have been scarce. With the current era of fiscal accountability, perfusion departments shy away from clinical evaluations and are susceptible to purchasing departments choosing cost over clinical performance value (7).

Recently, we undertook a clinical evaluation of the incumbent oxygenator and others newly available on the Canadian market (8). This small-scale evaluation found discrepancies in gas transfer, pressure gradients and effects on patient hematology (hemoglobin (Hgb) concentration, platelets, white blood cells (WBC) and neutrophils) and played a key role in determining the oxygenators our hospital went on to purchase. Further, this quality assurance

exercise afforded us the opportunity to develop and refine our oxygenator evaluation tools. In presenting the subsequent data and the importance of the process at national meetings, we attracted the attention of two other Canadian perfusion departments for a similar evaluation.

The goal of the current manuscript was to conduct a quality assurance evaluation at two other Canadian centers on their current oxygenators by assessing key metrics of gas exchange, pressure gradients through the oxygenator and effects on patient hematology. These data would then be compared, blinded,

Materials and Methods:

Three Canadian cardiac centres (St. John Regional Hospital (SJRH), New Brunswick, Nova Scotia Health Authority (NSHA), Nova Scotia and London Health Sciences Center (LHSC), Ontario participated in the current oxygenator evaluation. Ethical review board approval was obtained at each center for a quality assurance project between the three centers. For the purposes of presenting data in this manuscript, the identity of the hospitals is blinded. Instead, when the oxygenator data are delineated to describe center-specific experience (rather than pooled oxygenator data), data are labeled as oxygentor_1 and _2 (for example: Inspire_1 and Inspire_2). As part of a recent publication, NSHA conducted an evaluation of all new oxygenators available in Canada. For the current manuscript, the data on the LivaNova Inspire 8F (Inspire) (280 Hillmount Rd, Markham ON, Canada), Maquet Quadrox-i (Quadrox,) (90 Matheson Blvd, Mississauga, ON, Canada) and Terumo FX25 (FX25) (950 Elkton Blvd, Elkton, MD, USA) were included from the aforementioned publication. NB and LHSC evaluated their current oxygenators.

The goal of the current manuscript was to generate a large clinical database on three contemporary oxygenators based on the experience of 3 Canadian centers (approximately 3000 cases/year combined) in order to quantify key performance metrics: gas exchange, pressure gradients and impacts on blood cell components.

A complete description of the clinical measurements and analysis are published elsewhere[8]. Briefly, a comprehensive data collection form was used to collect data for each case similar to Stanzel and Henderson. Data captured included patient (height, weight, etc., but no patient identifiers), case demographics (type of case, pump and aortic cross clamp times, etc.), clinical data collected during routine blood gas analysis (arterial and venous samples) and pre-heparin/post cross-clamp complete blood cell counts (CBC). Arterial and venous blood gases were analysed in the operating room using GEM4000 (Instrumentation Laboratory, 180 Hartwell Road, Bedford, MA, USA) and CBC samples were analyzed at the institute's core laboratory facility. From these: *oxygen (O_2) transfer*, *sweep gas flow rate required for a carbon dioxide (CO_2) of 40 mmHg*, *pressure gradient through the oxygenator*, *hemoglobin/platelets/WBC and neutrophils percent pre-bypass* were calculated as previously described. No patient identifiers or outcomes were collected.

This was a not a randomized, controlled trial. For NS, it was a prospective, sequential evaluation with the goal of assessing 30 of each oxygenator as part of an evaluation to find a replacement product. For SJRH and

LHSC, this was a prospective sequential evaluation that collected data from cases over the course of 4 months (2016) with the goal of capturing data from approximately 100 cases per center.

Cases were conducted as using the established practices at each site. For Inspire_1, prime consisted of 700-1000 ml of PlasmalyteA, 500 ml Voluven®, 50 ml 8.4% sodium bicarbonate, 100 ml of 25% mannitol, and 10,000 units heparin. Accepted minimum activated clotting time (ACT) range was 400-480 seconds, target cardiac index was 2.4 L/min/m^2 and patient nasopharyngeal temperatures ranged from 28^{o}C to normothermia. Micro-cardioplegia was used. For Inspire_2, Quadrox_2 and FX25_2, prime consisted of 2 L of PlasmalyteA, 0.5 g/kg mannitol and 4 grams of cefazolin (if not contraindicated). Accepted minimum ACT was 480 seconds, target cardiac index was 2.4 L/min/m^2 and patient nasopharyngeal temperatures ranged from 32^{o}C to normothermia. 4:1 (blood: crystalloid) cardioplegia was used. For Quadrox_1 and FX25_1, 1300 ml Plasmalyte A, 200 ml of 20% mannitol and 10, 000 units heparin. Accepted minimum ACT was 480 seconds, target cardiac index was 2.4 L/min/m^2 and patient nasopharyngeal temperatures ranged from 32^{o}C to normothermia. Micro-cardioplegia was used.

The study design was observational. Inclusion criteria were all patients 18 years of age or older. Emergency cases were excluded. For O_2 transfer, only data collected when the patient nasopharyngeal temperature was 30^{o}C-37^{o}C were included, as patient temperatures below 30^{o}C were found in Stanzel and Henderson (data not shown) to impact venous saturations (increase due to reduced metabolic demand) and hence skew O_2 transfer analysis. For CO_2 analysis, data collected when CO_2 was used in the operative field (requirement for some surgeons for valve cases) were excluded. For Hgb analysis, any patients that received RBC transfusion intra-operatively were not included.

As this was a quality assurance evaluation, the standard of care at each center remained the same with no changes to clinical practice, with all perfusionists at each center collecting data. Perfusionists were randomized to oxygenators, based on their assigned operating room assignments.

All non-categorical data were evaluated using a one-way analysis of variance with *Bonferroni correction* for multiple measurements. Categorical data were analyzed using a *Fisher's exact test*. All data are presented as mean ± standard deviation. Statistical significance was set at $p < 0.05$.

Results:

There were no differences in patient, case or procedure demographics ($p > 0.05$) (Table 1).

Oxygen transfer: There was no variation in oxygen transfer (normalized to FiO_2) between oxygenators used at individual centers except Inspire_1 (Figure 1A). Inspire_1 had the lowest oxygen transfer (186 ml/min/FiO_2) of all oxygenators except FX25_2 ((208 ml/min/FiO_2), $p = 0.94$. FX 25_2 oxygen transfer was equivalent to the remaining oxygenators ($p > 0.05$). The remaining centers had equivalent oxygen transfer (Inspire_2 = 243 ml/min/FiO_2, Quadrox_1 = 235 ml/min/FiO_2, Quadrox_2 =

234 ml/min/FiO_2, FX_1 = 235 ml/min/FiO_2 ($p > 0.05$)).

When the data were pooled for each oxygenator (Figure 1B), the Inspire had the lowest oxygen transfer/FiO2 (199 ml/min/FiO_2, $p < 0.01$)), while Quadrox (228 ml/min/FiO_2) and FX25 (225 ml/min/FiO_2) were equivalent ($p = 1$).

(Figure 2A). Inspire_1 and 2 had the largest pressure gradients (30 and 27 mmHg/l/min, respectively), followed by FX_1 and FX_2 (13 and 11 mmHg/l/min, respectively) and the Quadrox_1 and Quadrox_2 had the lowest pressure gradients (10 and 8 mmHg/l/min, respectively) ($p < 0.05$). There was no variation in pressure gradients between centers ($p > 0.05$) using the same oxygenator. When the data were pooled, the Inspire had the largest pressure gradient (29 mmHg/l/min), followed by the FX25 (12 mmHg/l/min) then the Quadrox (9.0 mmHg/l/min) ($p < 0.05$) (Figure 2B).

Table1: Patient and procedure demographics

	Inspire_1	Inspire_2	Quadrox_1	Quadrox_2	FX25_1	FX25_2	p value
Number	94	30	24	28	70	28	> 0.05
Gender (% female)	27 ± 4.6	16.7 ± 6.9	9.1 ± 6.3	17.9 ± 7.4	28.6 ± 5.4	25 ± 8.3	> 0.05
Age (years)	63.8 ± 0.97	65.3 ± 1.59	69.1 ± 2.24	62.75 ± 1.47	65.5 ± 1.47	67.6 ± 1.81	> 0.05
Weight (kg)	86.3 ± 1.7	87.8 ± 3	88.8 ± 3.7	85.9 ± 3.1	87.3 ± 1.7	88.5 ± 2.8	> 0.05
BSA (m2)	2 ± 0.2	2 ± 0.2	2 ± 0.2	2 ± 0.2	2 ± 0.2	2 ± 0.2	> 0.05
Procedure Details							
Pump time (minutes)	106.8 ± 4.3	121.4 ± 7.6	115.4 ± 18	129.1 ± 10	116.3 ± 9.1	134.3 ± 11	> 0.05
Clamp time (minutes)	83.1 ± 3.7	88.1 ± 6.7	83.4 ± 9.2	94 ± 8	83.1 ± 6.8	93.7 ± 7.8	> 0.05
Operative Procedure (#(%))							
CABG	54(57)	15(50)	14(58)	15(54)	44(63)	11(39)	> 0.05
Isolated Valve	16(17)	6(20)	6(25)	7(25)	16(23)	8(29)	> 0.05
Combination	20(21)	4(13)	1(4.2)	3(11)	8(11)	6(21)	> 0.05
Aortic	1(1)	3(10)	0(0)	3(11)	1(1.4)	1(3.6)	> 0.05
Redo	1(1)	2(6.7)	3(12.5)	2(7.1)	1(1.4)	3(11)	> 0.05
Other (tx, ressection, etc.)	2(2.1)	1(3.3)	0(0)	1.(3.6)	0(0)	2(7.1)	> 0.05

Carbon Dioxide transfer: There was no difference in sweep gas flow rate required to achieve a partial pressure of arterial CO_2 ($PaCO_2$) of 40 mmHg between oxygenators used at individual centers ($p > 0.05$) except between Inspire_2 (0.051 l/min) and Quadrox_1 (0.66 l/min), $p = 0.001$ (Figure 1C). The sweep gas flow rate required for a $PaCO_2$ of 40 mmHg was 0.58 L/MIN, 0.57 L/MIN, 0.62 l/min and 0.57 l/min for the Inspire_1, Quadrox_2, FX25_1 and FX25_2, respectively. When the data were pooled for each oxygenator (Figure 1D), no differences were observed between oxygenators ($p = 0.058$).

Pressure gradient: The pressure gradient through the oxygenator (pre oxygenator minus post oxygenator, normalized to blood flow rate) varied between oxygenators

Hemoglobin: Hgb values post-cross clamp were normalized to pre-CPB values (Figure 3A). The only significant difference observed between centers was Inspire_1 (72% of baseline) and FX_1 (77% of baseline) ($p = 0.008$). The other normalized Hgb values were 74, 78, 78 and 76% of baseline for Inspire_2, Quadrox_1, Quadrox_2 and FX_2, respectively. When the data were pooled for each oxygenator (Figure 3B), the Inspire had the lowest post clamp Hgb (73 % baseline, $p < 0.05$). The Quadrox (78 % baseline) and FX25 (77 % baseline) were equivalent ($p = 1$).

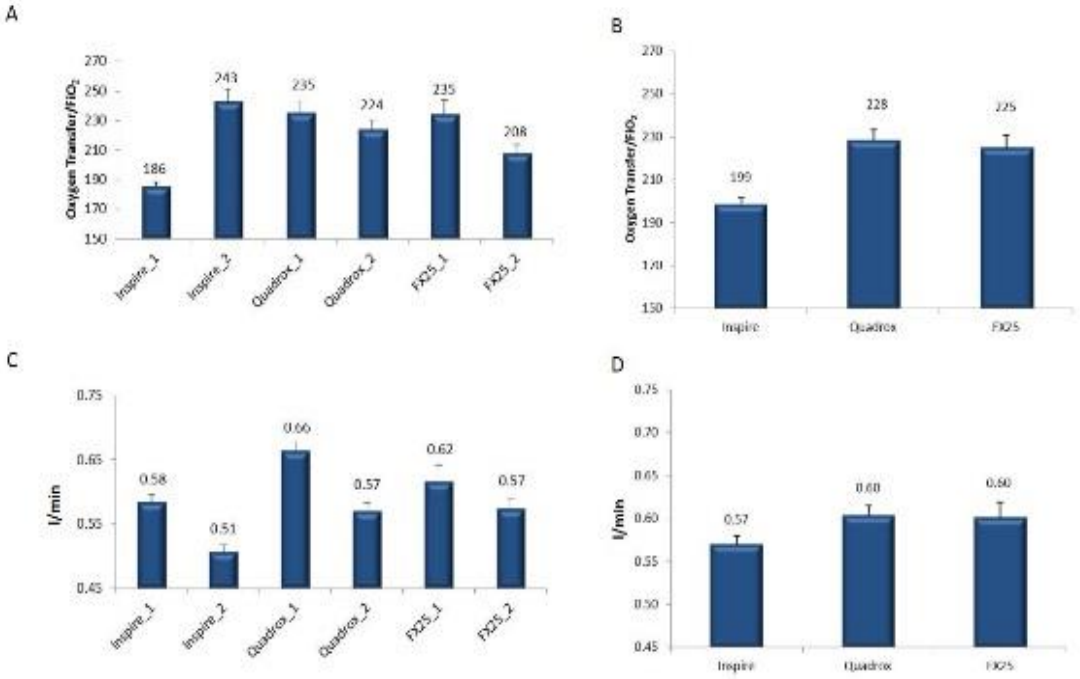

Figure 1: Gas transfer. There was no variation in oxygen transfer (normalized to FiO_2) between oxygenators used at individual centers except Inspire_1 (Figure 1A). When the data were pooled for each oxygenator (Figure 1B), the Inspire had the lowest oxygen transfer. There was no difference in sweep gas flow rate required to achieve a $PaCO_2$ of 40 mmHg between oxygenators used at individual centers ($p > 0.05$) except between Inspire_2 and Quadrox_1 (Figure 1C). When the data were pooled for each oxygenator (Figure 1D), no differences were observed between oxygenators.

Platelet counts: Platelet counts post-cross clamp were normalized to pre-CPB values (Figure 3C). FX25_1 had the largest platelet retention (88%, $p < 0.01$). Platelet retention for the other centers was 79, 73, 78, 77 and 74% of pre-CPB values for Inspire_1, Inspire_2, Quadrox_1, Quadrox_2 and FX25_2, respectively and there was no variation between these values. When the data were pooled for each oxygenator (Figure 3D), FX25 had the largest platelet retention (85% of baseline value, $p < 0.001$). Inspire and Quadrox were equivalent (both 77% of baseline value).

White blood cell counts: WBC counts post-cross clamp were normalized to pre-CPB values (Figure 4A). FX25_1 (172% baseline) had larger WBC proliferation than Inspire_1 (135% baseline, $p = 0.002$), Quadrox_2 (114 % baseline, $p = 0.001$) and F25_2 (98 % baseline, $p < 0.001$). Quadrox_1 (160 % baseline) had greater WBC proliferation than FX25_2 ($p = 0.016$). Inspire_2 (141% of baseline) was not different than any other oxygenator ($p > 0.05$). When the data were pooled for each oxygenator (Figure 4B), there were no differences between Inspire (136% of baseline), Quadrox (134% of baseline) and FX25 (155% of baseline), $p > 0.05$.

Neutrophil counts: Neutrophil counts post-cross clamp were normalized to pre-CPB values (Figure 4C). Quadrox_2 (122% of baseline) and FX25_2 (123% of baseline) had the lowest neutrophil values ($p < 0.05$). Inspire_1 (165% of baseline), Inspire_2

(185% of baseline) and FX25_1 (218% of baseline) were equivocal ($p > 0.05$).

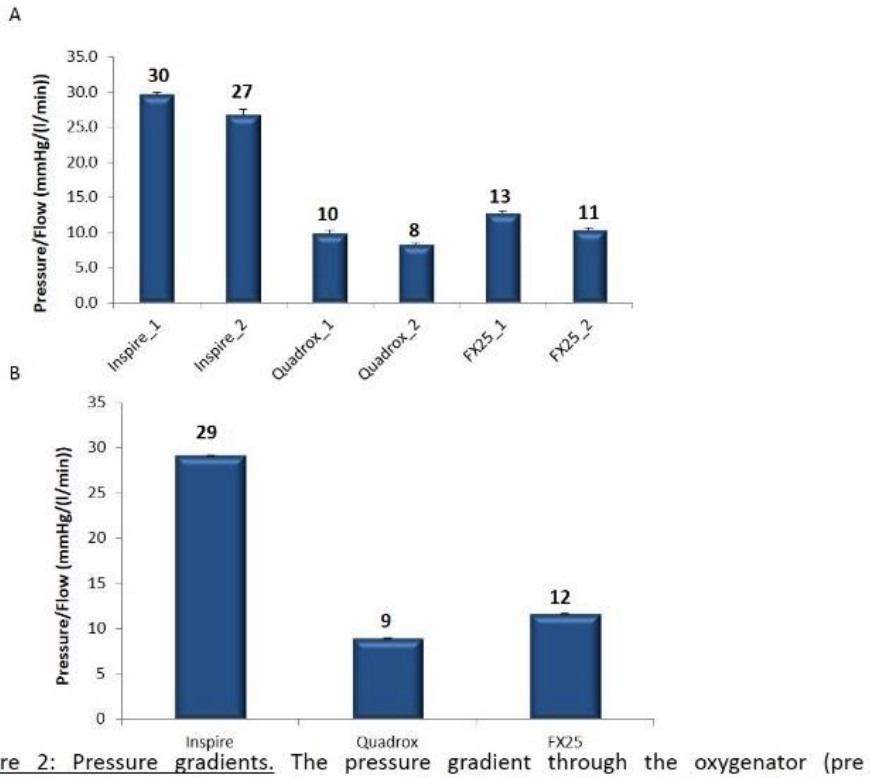

Figure 2: Pressure gradients. The pressure gradient through the oxygenator (pre oxygenator minus post oxygenator, normalized to blood flow rate) varied between oxygenators (Figure 2A). Inspire_1 and 2 had the largest pressure gradients followed by FX_1 and FX_2 and the Quadrox_1 and Quadrox_2 had the lowest pressure gradients. There was no variation in pressure gradients between centers using the same oxygenator. When the data were pooled, the Inspire had the largest pressure gradient, followed by the FX25 then the Quadrox.

Neutrophil data of Quadrox_1 were not collected.

When the data were pooled for each oxygenator (Figure 4C), Quadrox had the lowest neutrophil value (122% of baseline) ($p < 0.05$), while Inspire (169% of baseline) and FX25 (179% of baseline) were equivalent ($p > 0.05$).

Discussion:

While there have been a number of single center oxygenator evaluations (3,7,9,10), the current manuscript represents the *first multi-centre* evaluation of these contemporary oxygenators and compared data to a small, single center trial that was recently published with a combined caseload between the three centers of approximately 3000 cases per year. The data from the current manuscript demonstrate disparities in a number of performance metrics measured both between the different oxygenators, as well as the same oxygenator at different centers (e.g. Inspire_1 vs Inspire_2). While the former was expected based on both performance data provided by the manufacturers and the recent evaluation by Stanzel and Henderson, the later was not.

Of particular interest, was disparity in gas exchange between the two centers with the Inspire.For the former metric, oxygen transfer was normalized by FiO_2, with oxygen transfer being the difference between arterial and venous oxygen content. Any factor affecting these two will impact oxygen transfer with factors increasing arterial content or decreasing venous content contributing to increased transfer (11). While the oxygen saturation of blood leaving the oxygenator is expected to be close to 100%, this leaves only Hgb and partial pressure arterial of oxygen (PaO_2) to vary.

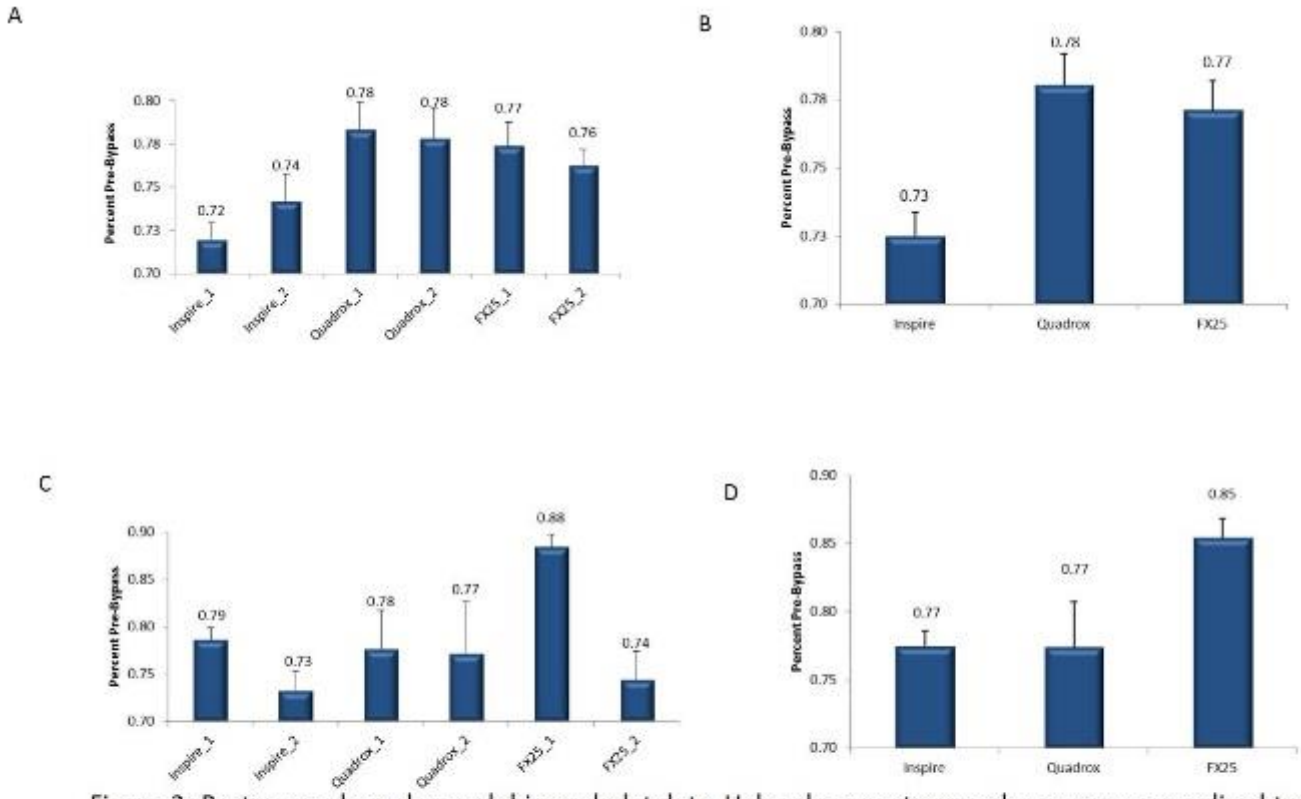

Figure 3: Post-cross clamp hemoglobin and platelets. Hgb values post-cross clamp were normalized to pre-CPB values (Figure 3A). The only significant difference observed between centers was Inspire_1 and FX_1. When the data were pooled for each oxygenator (Figure 3B), the Inspire had the lowest post clamp Hgb. The Quadrox and FX25 were equivalent. Platelet values post-cross clamp were normalized to pre-CPB values (Figure 3C). FX25_1 had the largest platelet retention. When the data were pooled for each oxygenator (Figure 3D), FX25 had the largest platelet retention. Inspire and Quadrox were equivalent.

Since arterial and venous Hgb are expected to be equivalent, the only factor affecting the oxygen content in blood leaving the oxygenator is PaO_2, which is affected by the FiO_2 used by the perfusionist. In our calculation, FiO_2 was factored into the equation. Therefore, differences in venous blood may be responsible and any increase in patient metabolism may play a role in venous blood oxygenation. One such factor is the anesthesia level of the patient, which was not captured in the current manuscript. If this was accurate, then we would expect that the patients with Inspire_1 were more deeply anesthetised resulting in reduced oxygen consumption, higher venous saturations and hence less capacity for oxygen transfer. A *post-hoc* analysis of the raw data demonstrated that the mean SvO_2 for Inspire_1 was 83.4%, while that of Inspire_2 was 81%, representing a significant difference ($p < 0.005$). While patient sedation was not captured, rendering this hypothesis impossible to prove unequivocally, patient nasopharyngeal temperature was captured. In a further *post-hoc* analysis of these data, the mean patient nasopharyngeal temperature for Inspire_1 was 33.6°C while Inspire_2 was 34.1°C ($p = 0.023$). This minor difference *may* contribute to the explanation for the reduced O_2 transfer with the Inspire_1 as this *may* be influence patient metabolic rate. Another factor that could affect venous oxygen

content could be pump flow rate. Analyzing the cardiac index used at the different centers during the cases did not provide evidence of variation ($p > 0.05$, data not shown).

Likewise, Inspire_1 and Inspire_2 showed variation in CO_2 transfer efficiency (sweep gas flow rate required to obtain a $PaCO_2$ of 40 mmHg). The difference in CO_2 transfer seems at odds with the sedation hypothesis posited above. In that hypothesis, Inspire_1 patients were more deeply anesthetised, resulting in reduced metabolic demand. Based on this, CO_2 generation would also be reduced, resulting in less sweep gas flow rate needed to achieve a $PaCO_2$ of 40 mmHg. This was not the case, as Inspire_1 patients required a greater sweep gas flow rate. As with O2 transfer, a reduction in patient nasopharyngeal temperature may impact metabolic rate and influence CO_2 production.

Unlike gas exchange, pressure gradients data between centers was consistent and differences between oxygenators were similar to that observed previously (8) and in line with published data from the manufacturers (4,5,6).

The effects of an oxygenator on hematology is often overlooked in terms of evaluating oxygenator performance. While the effects of CPB on hematology is multi-faceted, being influenced by not only the oxygenator, but the intrinsic tubing coating, hemodilution, surgical and anesthesia practice, etc, the authors believe this is a key metric to consider. It was interesting to note that Inspire resulted in the lowest Hgb values post cross clamp removal. Numerous studies have underscored the importance of reducing hemodilution on CPB as a means of reducing the risk of blood transfusions (12,13). While there are differences in prime volumes of the oxygenators themselves, for example 260 ml for FX25 and 352 mL for Inspire, when the entire CPB circuit is included in, there is little difference in prime volume (i.e. 1236 ml for FX25 and 1270 for Inspire) (Stanzel and Henderson). The differences may not appear substantial (73 vs 78 and 77 % of pre-CPB Hgb for Inspire, Quadrox and FX25 respectively), however, such differences could clinically impact patients in terms of need for blood transfusion during their *entire* stay in hospital. This was not recorded in the present manuscript as outcomes were beyond the scope of the obtained ethics approval. An additional consideration for Hgb levels is the myocardial protection strategy as not all centers used microcardioplegia. However, as Inspire_1 used a microcardioplegia strategy, while Inspire_2 used 4:1 cardioplegia, which would result in greater hemodilution. Another potential cause could be the use of Voluven®, a volume expander, in the prime solution for Inspire_1. As a volume expander, Voluven® would effectively increase the patient's intravascular volume and hence could result in an exaggerated hemodilution.

In terms of platelets, FX25_1 and FX25 (pooled data) demonstrated the greatest retention. It is unclear to the authors the underlying explanation for this finding. Of interest, FX25_2 used a LivaNova circuit (P.h.i.s.i.o. coating), while the FX25_2 used a Terumo circuit (X-Coating™). A number of studies have investigated the various CPB coatings available, largely designed to show non-inferiority and no superior coating has been identified to date. It is also important to note that these findings represent platelet

number and not function. This aspect of the evaluation would have benefited from use of a platelet function tool, such as PlateletWorks® (14).

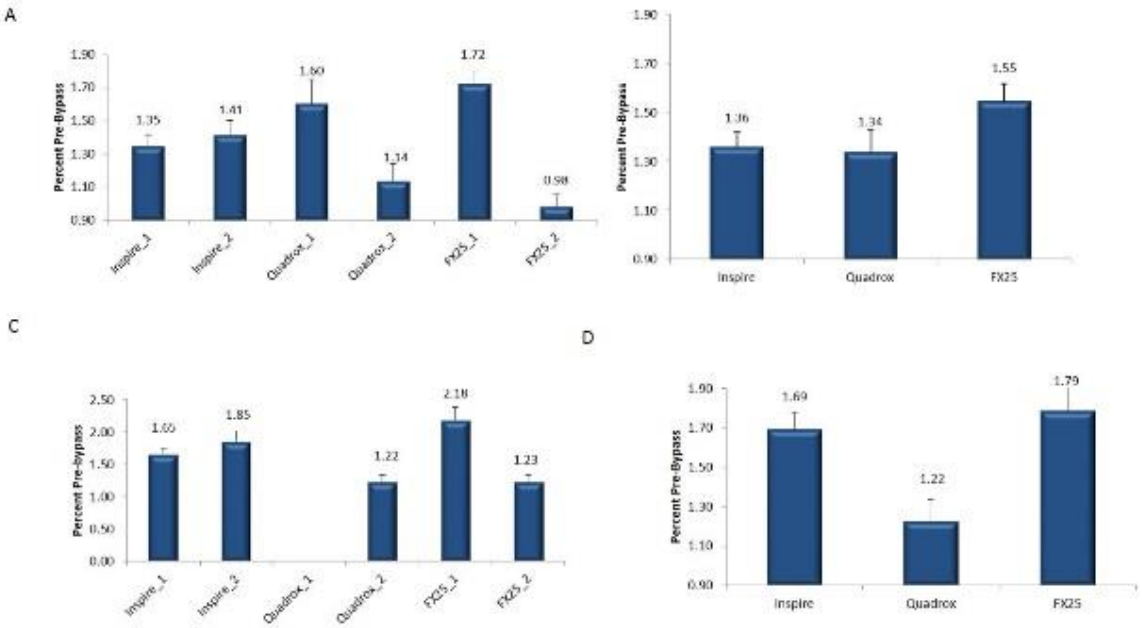

Figure 4: Post cross-clamp immune cells. WBC values post-cross clamp were normalized to pre-CPB values (Figure 4A). FX25_1 had larger WBC proliferation than Inspire_1, Quadrox_2 and F25_2. Quadrox_1 had greater WBC proliferation than FX25_2. Inspire_2 was not different than any other oxygenator. When the data were pooled for each oxygenator (Figure 4B), there were no differences between oxygenators._Neutrophil values post-cross clamp were normalized to pre-CPB values (Figure 4C). Quadrox_2 and FX25_2 had the lowest neutrophil values. Inspire_1, Inspire_2 and FX25_1 were equivocal. Neutrophil data of Quadrox_1 were not collected.
When the data were pooled for each oxygenator (Figure 4C), Quadrox had the lowest neutrophil value, while Inspire and FX25 were equivalent.

When WBC were quantified, a number of differences were observed between oxygenators at the different centers that were ultimately nullified when data were pooled for each oxygenator. For example, FX25_1 had the largest increase in WBC (equivalent to Quadrox_1), while FX25_2 was equivalent to the baseline WBC level. Is it possible that while the X-Coating® on the entire FX25_1 CPB circuit may have beneficial for platelet retention that it was responsible for WBC activation and proliferation? Again, these differences in circuit coating have not been well-elucidated in terms of clinical outcomes (15) and no comprehensive evaluation of commercially available coatings on immune cell proliferation has been published to-date. A similar trend was observed for neutrophil numbers. Clearly, the intricacies of the immune system and especially in response to CPB are complex and incompletely understood (16, 17). An interesting hypothesis for the differences in FX25 at the different centers is the fact that CO_2 was introduced into the surgical field for a greater proportion of FX25_1 cases than FX25_2 cases. When the FX25_1 centre evaluated their own data to determine a cause for this increase in WBC proliferation, it was noted that there appeared to be a relationship between the use of CO_2 in the operative field and increased WBC proliferation. While the data did not prove a direct cause and effect in a relatively small

sample size, it did result in further investigation which revealed that use of CO_2 into the operative field resulted in acidosis of the blood being returned from the chest cavity by pump suckers and vents. Work elsewhere has revealed evidence for acidosis-induced activation of immune cells (18). In the cases in which this was examined, the pH of this blood was typically 7.0 or below despite a normal pH of the venous blood, suggesting that suction and vent return from the field was very acidic. This was a limited investigation and requires further work to elucidate a possible relationship between CO_2-induced acidosis and immune cell proliferation.

Not only does this manuscript represent the first multi-centre evaluation of these contemporary oxygenators, it also permitted the participating centers to establish the baseline level of care provided with these products and a starting point for the participating centers to optimize their perfusion practice. The authors propose that perfusion departments consider conducting similar quality assurance initiatives to examine performance of their current oxygenator, as well as new oxygenators on the market that may replace their existing products when the time comes. It was noted by Stammers *et al* that perfusionists often rely on anecdotal information on oxygenator performance such as vendor-supplied white papers and that hospitals often do not have the necessary resources to conduct preclinical evaluations on oxygenators (7). In the current manuscript, gas exchange was an inexpensive evaluation, requiring only the time of the perfusionist to run a venous gas for every arterial gas to determine O_2 transfer and some 'office time' to compile and analyse the resulting data. The CBC data, while inherently interesting, requires extra resources and collaboration with the central lab. By participating in such initiatives, we are arming ourselves with the best scientific evidence for the oxygenators we purchase, rather than leaving the decision to cost instead of value. If we do not ask the questions, then we do not know the level of care we are providing our patients.

<u>Limitations</u>:
This observational study represents the first multi-centre evaluation of these contemporary oxygenators and permitted the participating centers to assess the baseline level of care provided with these products. The established baseline serves as a starting point for the participating centers to optimize their perfusion practice. However, there are a number of limitations and considerations that need to be highlighted.

This manuscript was a quality assurance initiative which reflected the current practice at each site. As such, the practices of anesthesia and perfusion were not standardized across the centers resulting in the potential for a number of confounding variables including the large number of perfusionists involved (30 total). The use of multiple statistical analysis in this evaluation may also contribute to the potential for statistical bias.

While these data represent the evaluation of a number of each oxygenator, there is variability in the actual number of each oxygenator evaluated (range: 24 Quadrox_1 to 94 Inspire_1). Ideally, 100 of each oxygenator (the total number of evaluations approved by the institutes' ethics committee) at each center would have been evaluated to provide the more

representative data, but due to departmental constraints this was not feasible.

Further, patient demographics collected were limited to gender, age and size, as per ethics. This overlooks a number of key pre-existing factors such as diabetes and organ dysfunction, which may contribute to outcomes such as immune cell proliferation. As well, intra-operative outcomes including hyperlactemia, hyperglycemia, hemolysis, creatinine and organ function which may be indicators of oxygenator function were not collected (8).

Conclusions: This multicenter evaluation of contemporary oxygenators evaluated gas exchange, pressure gradients and effects on patient hematology during CPB. There was heterogeneity in gas exchange both between different oxygenators and the same oxygenator at different centers. Pressure gradients also varied among oxygenators with Inspire having the largest gradient pre to post oxygenator. The Inspire oxygenator had the largest drop in Hgb, while FX25 had the greatest platelet retention. Despite equivalency between oxygenators in terms of WBC proliferation, there was heterogeneity between FX25 used at two centers. These observed differences support the need for perfusion departments to conduct their own quality assurance evaluations in order to better understand the care they are providing their patients with ongoing goal of optimizing perfusion care.

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