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MAIN TEXT

Venous chambers in clinical use for hemodialysis have limited capacity to eliminate microbubbles from entering the return bloodline: An in vitro study

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Abstract

Background: During hemodialysis (HD), blood passes through an extracorporeal circuit (ECC). To prevent air administration to the patient, a venous chamber (chamber) is located before the blood return. Microbubbles (MBs) may pass through the chamber and end up as microemboli in organs such as the brain and heart.

This in vitro study investigated the efficacy of various chambers in MB removal.

Materials and Methods: The in vitro recirculated setting of an ECC included an FX10 dialyzer, a dextran-albumin solution to mimic blood viscosity and chambers with different flow characteristics in clinical use (Baxter: AK98 and Artis, Fresenius: 5008 and 6008) and preclinical test (Embody: Emboless®). A Gampt BCC200 device measured the presence and size of MBs (20–500 μm). Percentage change of MBs was calculated: ΔMB% = 100*(outlet–inlet)/inlet for each size of MB. Blood pump speed (Qb) was 200 (Qb200) or 300 (Qb300) ml/minute. Wilcoxon paired test determined differences.

Results: With Qb200 median ΔMB% reduction was: Emboless −58%, AK98 −24%, Fresenius 5008 −23%, Artis −8%, and Fresenius 6008 ± 0%. With Qb300 ΔMB% was: Emboless −36%, AK98 ± 0%, Fresenius 5008 ± 0%, Artis +25%, and Fresenius 6008 + 21%. The Emboless was superior to all other chambers with Qb200 and Qb300 ($p < 0.001$). Further, the Emboless with Qb300 still eliminated more MBs than all other chambers with Qb200 ($p \leq 0.003$).

Conclusion: The results from the present study indicate that flow characteristics of the chamber and the Qb are important factors to limiting exposure of MB to the return bloodline. The Emboless chamber reduced MBs more effective than those chambers in clinical use investigated.

KEYWORDS

air bubbles, emboli, extracorporeal circuit, hemodialysis, regulations, safety, safety risk, venous chamber

1 | INTRODUCTION

During hemodialysis (HD), blood drawn from a vascular access will be pumped through an extracorporeal circuit (ECC) as part of the dialysis device. The ECC consists of disposable polyvinylchloride tubes including a pump segment (the arterial line) that is connected to the dialyzer. After the blood is rinsed from waste substances within the dialyzer, it exits into a return bloodline system of the ECC (the venous line) that leads through a venous chamber (air trap) and then back into the patient through a return vascular access. On the ECC bloodline, several connecting tubes enable pressure control and the addition of anticoagulants, drugs, and fluid. As the ECC and the dialyzer (usually) are stored dry, a priming procedure is performed to eliminate air from the ECC before blood enters the system. Such priming is done by perfusion of the system with either saline or dialysis fluid manually or automatically. Nevertheless, after priming, the ECC contains some residual air.[1,2] If a leakage in a connection occurs at the site before the blood pump a negative pressure causes air to be sucked into the bloodline.[3–5] Incorporated in the bloodlines is a venous chamber. This chamber also includes the safety function of measurement of venous blood pressure without blood contamination of the pressure gauge. One way to accomplish the venous chamber and pressure measurement are through a pod with a water-impermeable membrane. Another important safety function is that of an air trap that enables evacuation of air contamination to avoid air returning back into the patient. The shape of venous chambers as well as the flow characteristics differ with the intent to avoid air contamination. In addition, an air detector is incorporated in the venous chamber to stop blood flow and gives an alarm if air contamination occurs.

Despite safety measures, in vitro and clinical studies have shown that microbubbles (MBs) of air pass through the venous chambers without inducing an alarm and these return into the venous bloodline of the patient.[2,4,6–8] The amount of MBs increase with the blood pump speed,[7,9] and is dependent on priming mode and dialyzer membrane condition such as during hemodiafiltration.[1] In vitro studies show that MB exposure differs between venous chambers.[8]

However, MBs have been detected in autopsies of dialysis patients, not only in the lungs but also in tissue such as the brain and heart.[10–12] This indicates that the MBs are not fully adsorbed within the blood but instead may cause microemboli and subsequent lesions. These previous studies point out that microemboli are induced by air bubbles that enter the blood and may be deposited in organs because of contamination during medical care especially hemodialysis.[12] These new risk data are learned from autopsy. According to the IEC 601-2-16:2018 guidelines, each manufacturer is responsible for their respective device regarding the elimination of air contamination (IEC 601-2-16:2018). The standard for risk management for medical devices encourages manufacturers to identify, analyze, and control risks (ISO 14971). Identified risks should be reduced to acceptable levels or as far as reasonably possible include a warning in instructions for use.[13]

However, as the manufacturers do not provide data of such micro air contamination, and as there is no study comparing the different bloodlines, we felt it important to investigate these conditions. To allow similar conditions for comparing various venous chambers, an in vitro setting was deemed best suitable.

The aim of this study was to investigate the efficacy of MB elimination of venous chambers that have different flow characteristics and are used in clinical practice or investigated preclinically.

2 | MATERIALS AND METHODS

2.1 | Experimental setting

Based on previous clinical data on HD with the Fresenius 4008 venous chamber, a median of 3263 MBs entered the return line of the ECC of those patients during 180 min of HD.[9] Therefore, we aimed to make a model that provoked at least 3000 MBs at 6 min. This was achieved using a Fresenius 4008 dialysis device with an adjacent arterial pump segment and an FX10 dialyzer, initially primed with 500 ml fluid and with no dialysate connected. Follow-up monitoring of the MB frequency/second was used to determine when priming of a new dialyzer was necessary.

For the experimental set-up, a Fresenius 4008 dialysis device was used and was set in calibration mode, "check blood pump", to allow circulation of fluid flow without alarms or interruption. Experiments were performed at room temperature (21°C).

A 2-liter bag of fluid was prepared to mimic blood viscosity (B-SOL) according to Jonsson et al.[6] as follows: sterile priming solution of saline (Fresenius Kabi AB, Uppsala, Sweden) was mixed with Dextran T70 (Pharmacosmos A/S, Holbaek, Denmark) to a final concentration of 4% and human sterile albumin (Albunorm 200 g/L, Octapharma AB, Sweden) to a final concentration of 10 g/L.

A recirculating in vitro HD setting was established based on Fresenius bloodline LifeLineBeta for 4008 that included a 2 L B-SOL bag, blood pump, dialyzer, and venous line tubes in six branches. Five circuits included different venous chambers (Figure 1) and one circuit was a bypass line. The venous chambers (chambers) investigated had different flow characteristic concepts of air removal (Figure 2). The branches of the line in six branches were consequently

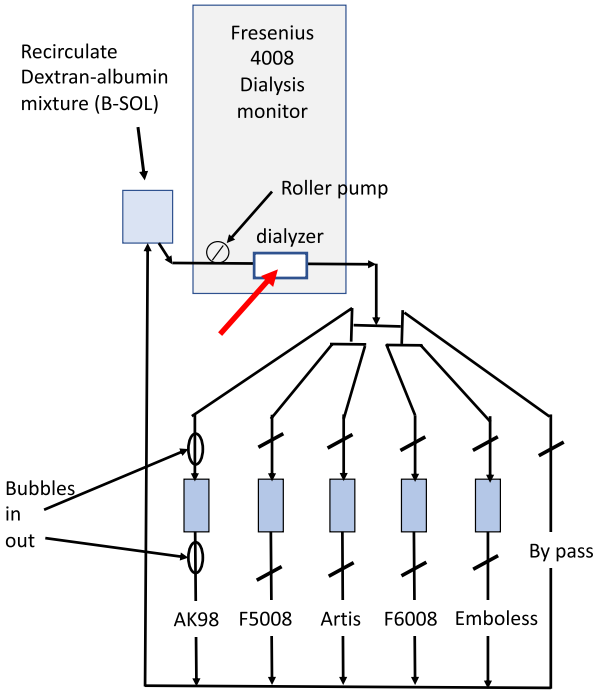

FIGURE 1 Setting of the in vitro system for investigation of air trap efficacy. The Fresenius 4008 dialysis monitor was used (open square). An intermediate bag was used for recirculation of a fluid that contained a dextran-albumin-mixture (B-SOL). The fluid was recirculated through the dialyzer (here FX10) corresponding to a 500 ml priming volume. The dialyzer was not connected to the dialysate. The red arrow indicates that residing air bubbles in the dialyzer were provoked to enter into the fluid within the tubes representing the extracorporeal bloodline system. This was done by a short knock on the dialyzer at specific time intervals. [Color figure can be viewed at wileyonlinelibrary.com]

made using similar T-shape couplings. Clamps were used at inlet and outlet lines to switch the flow between the six branches to allow a remaining recirculation.

The branches were made by T-coupling pieces of venous bloodlines and connections to venous chamber lines by cutting and with a fixation collar on the outside of the tubes. The original venous part of each bloodline was cut before and after the venous chamber and connected to the line as shown in Figure 1.

The different bloodlines could thereby be perfused by the same fluid mixture (B-SOL described above). The flow direction between the six branches was decided by open versus closed clamps. The setting allowed recirculation of the same fluid through all branches, which allowed the same conditions for the different venous chambers.

2.2 | Venous chambers investigated

The investigation included sterile venous bloodlines (Figure 2, Table S1 Supplement) for clinical use ArtiSet for the dialysis systems Gambro Artis (Artis) and AK 95/96/200/ultra/AK98 (AK98) by Baxter (Baxter Inc, Chicago, USA), and from Fresenius (Fresenius AG, Bad Homburg, Germany) the Lifeline Beta AV-set tonline-plus 5008-R (F5008) for 4008 and 5008 devices and the 6008 Careset BVM for 6008 devices (F6008). In addition, tests also included a bloodline (for preclinical use) with a specific venous chamber (Emboless) aimed to reduce MBs (Embody AB, Umea, Sweden; Emboless™, patented EPO10794463.9, SE536054 C2; US8894749B2; Ind 354482).

2.3 | Design of setting

Based on previous studies, it was known that air resided in the dialyzer despite priming and contaminating perfusing blood or fluid with MBs.[1,14] Therefore, the experiments included a dry stored dialyzer, hereby polysulfone and with a surface area of 1.8 sqm (FX10 by Fresenius AG, Bad Homburg, Germany). The dialyzer was inserted into the circuit. The bloodline before the dialyzer constituted the arterial part, and the bloodline after the dialyzer constituted the venous part where the venous chambers were inserted. To avoid dilution or viscosity changes, the dialysate fluid system was not connected, and the couplings were plugged. The recirculating system was "primed" and recirculated by the B-SOL fluid including all six branches (Figure 1).

A specially developed MB detector by GAMPT (Gampt BCC200 device, Germany) was placed on the circuit on the inlet line (MB_{inlet}) just before the entry of the venous air trap. A second MB-detector was placed on the circuit close to the outlet line of the venous chamber (MB_{outlet}). Both detectors were placed to the greatest extent in a vertical position to optimize measurement by the spread of MBs over the whole lumen of the flow of B-SOL.

Then perfusion of the particular (selected by randomization) venous chamber bloodline was initiated. The speed of the blood pump (Qb) was set to either 200 ml/minute (Qb200) or 300 ml/min (Qb300). These choices were based on the blood flow used in Europe and Japan as described in the DOPPS study[15] and the effect of pump speed on MBs.[9] The fluid level in the respective air traps were set at the level recommended by the respective manufacturer. If such recommendations were not given, we chose a high level (for AK98 and F5008). Based on our previous studies, a high level would represent optimal conditions for such chambers.[16]

When this was set, the experiments were started and the blood pump recirculated the B-SOL fluid through the system. Retained air in the dialyzer was released into the B-SOL circuit by provocation, by the same person, with a

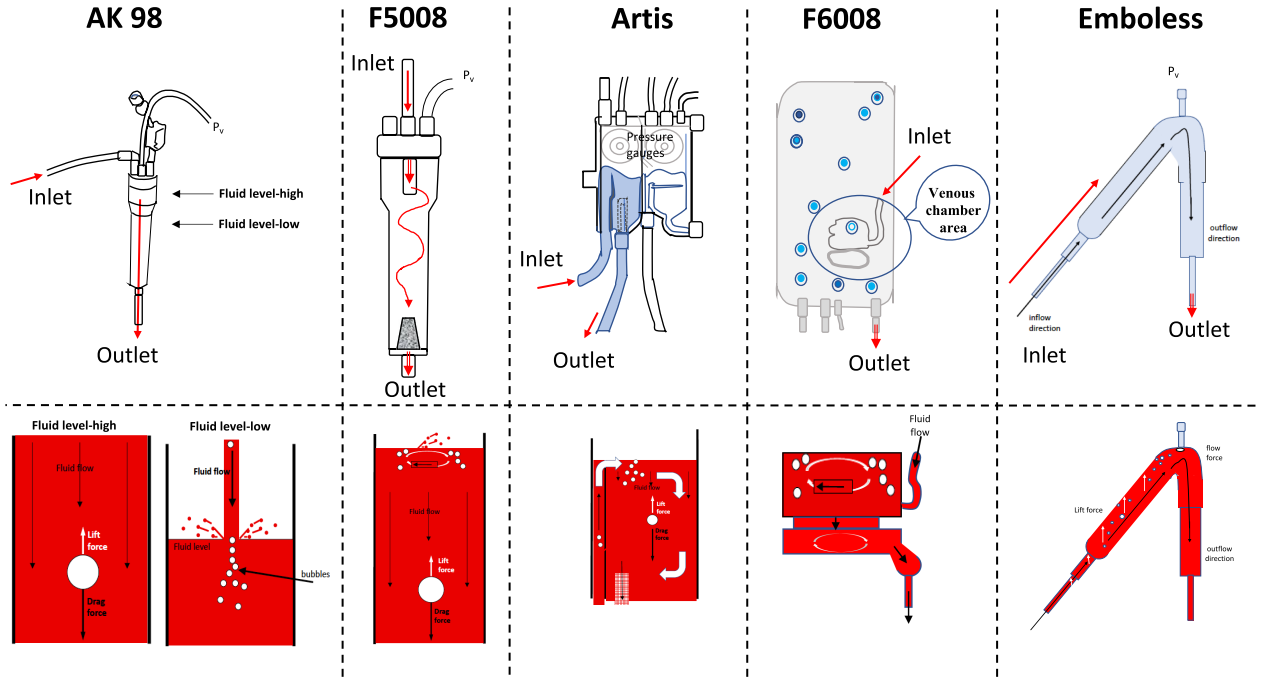

FIGURE 2 At the top are schematic descriptions of the various venous chambers and below are descriptions of flow characteristics in the chambers. Each chamber design is given above, and the flow characteristics are given below. For AK98 two characteristics are given, such as left side with a high fluid level and right side with a low fluid level. The F5008 generates a vortex such as the F6008. The Artis cartridge contains both an arterial (white) and venous (blue) chamber. The Fresenius 6008 cartridge includes an area indicating where the venous chamber is located. The sizes of the chambers are not proportionate. The air/fluid level on the Emboless chamber was set close to or just below the junction of the air exit tube from the chamber depending on peristaltic pressure motion. [Color figure can be viewed at wileyonlinelibrary.com]

short knock on the dialyzer. This induced flushes of MBs of air that contaminated the B-SOL circuit. This air contamination was induced by intermittent provocation three times during the 6 min perfusion session. The provocation was performed after 30 s, 2 min, and 4 min of perfusion. The initial and final periods of the 6 min were unprovoked as much as possible to achieve balanced inlet and outlet conditions in the venous chamber.

2.4 | Data analyses and calculation of inlet versus outlet microbubbles

The bubble counter (GAMPT BCC200) was used to measure the MB size between 20 and 500 μm diameter for each size, respectively. The total number of MBs achieved was calculated during a 6 min observation period. The system contained data of the number of counts for each size at the inlet (MB_{inlet}) and at the outlet (MB_{outlet}). The efficacy to eliminate MBs was calculated by the change in MB in percentage (ΔMB%) between outlet minus inlet according to the formula below:

$$\Delta MB\% = 100 \times \left(MB_{outlet} - MB_{inlet}\right) / MB_{inlet} \quad (1)$$

A reduction of MBs would be:

Given $MB_{inlet} = 20$ and $MB_{outlet} = 10$, Equation (1) results in

$$\Delta MB\% = 100 \times (10 - 20) / 20 => \Delta MB\% = -50\%, \quad (2)$$

A net increase of MBs at the outlet versus inlet may be due to: (1) splitting of large MBs into several smaller, or (2) the addition of bubbles from air within the chamber, or both (1) and (2).

Given $MB_{inlet} = 20$ and $MB_{outlet} = 40$, Equation (1) results in

$$\Delta MB\% = 100 \times (40 - 20)/20 => \Delta MB\% = +100\%, \quad (3)$$

2.4.1 | Imputations

If MB counts were present at outlet but no MB count was present at inlet the percentage change in MB was set as 100% increase. This was done by entering half of the value of the outlet to the inlet value up to a maximum MB_{inlet} of 2. A maximum of 100% MBs could be removed while additions of MBs could exceed 100%. The median values of percentage change were calculated for

diameter size 20–39 µm (group 20), 40–59 µm (group 40), 60–79 µm (group 60), 80–99 µm (group 80), 100–119 µm (group 100), 120–139 µm (group 120), 140–159 µm (group 140), 160–179 µm (group 160), 180–199 µm (group 180), 280–299 µm (group 280), 300–349 µm (group 300), 350–399 µm (group 350), and 400–500 µm (group 400). Sizes above 300 µm have a wider group range due to lower count of large bubbles. If no inlet and no outlet counts were present, the specific size was erased- censored-. The number and total volume (in nL) of MBs of each size were calculated as a mean of all five series of data and calculated as percentage proportion of the whole exposure in numbers and in volume. Also calculated was cumulative numbers (Figure 3A,B).

2.5 | Statistical analyses

Comparisons were performed between the change in percentage of outlet versus inlet counts at 6 min for the total MBs and for the different sizes. The size ranges used were "small" (20–199 µm diameter), "medium" (200–299 µm), and "large" (300–500 µm). Analyses were done between different venous chambers using non-parametric

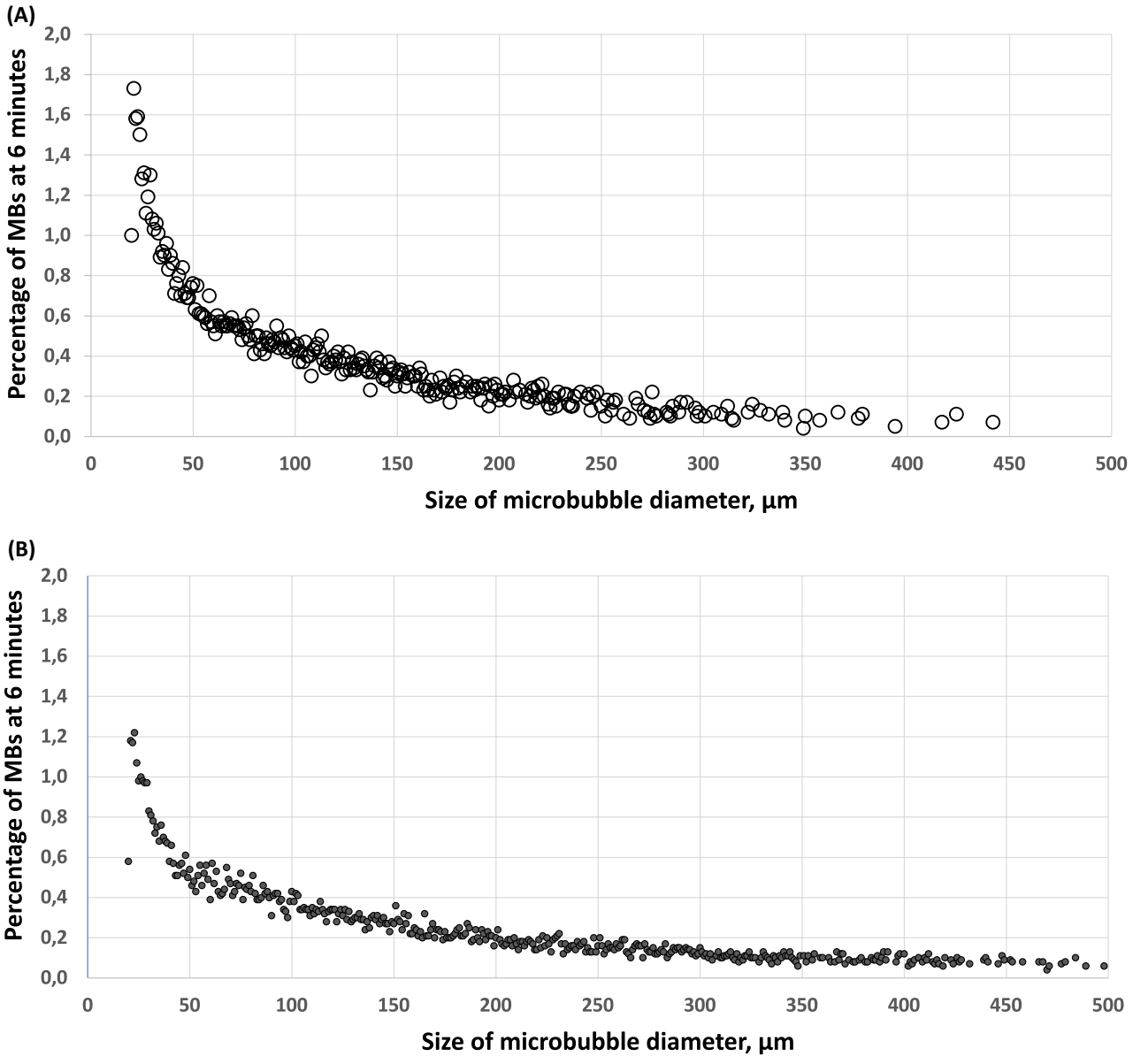

FIGURE 3 Microbubble (MB) results at 6-min exposure at the inlet line to the venous chamber are shown as the mean number for each MB size (20–500 µm diameter) of the five different series. Results are given as percentage of MBs of the total at various sizes at 6 min using either a blood pump speed of (A) 200 ml/minute (Qb200, open circles), or (B) 300 ml/minute (Qb300, filled circles). [Color figure can be viewed at wileyonlinelibrary.com]

Wilcoxon paired analyses. Thereby, the same MB sizes were compared between different venous chambers. A two-tailed value of $p < 0.05$ was defined as significant.

3 | RESULTS

The release and distribution of MBs from the dialyzer during the 6 min experiments with various blood pump speeds are given in Figure 3A,B. The figures show the distribution of all inlets measured MBs and in percentage related to their MB diameter size. A larger number of smaller bubbles were present with declining proportion toward fewer larger bubbles. The volume effect was inverse (not shown).

Comparison of change in the total MBs reduction capacity between various venous chambers is given in Table 1 and Supplement Table S2. Using Qb200 ml/minute the best median % change was achieved with Emboless versus all other chambers ($p < 0.001$). The median reductions of MBs were as follows: Emboless: −58%, AK98: −24%, Fresenius 5008: −23%, Artis: −8%, and Fresenius 6008: ±0%. Using Qb300 ml/minute the best median % change was achieved with Emboless versus all other chambers ($p < 0.001$). The median changes of MBs were as follows: Emboless −36%, AK98 ± 0%, Fresenius 5008 ± 0%, Artis +25%, and Fresenius 6008 + 21%. The increase in Qb from 200 ml/minute to 300 caused a significant lowering in the elimination of MBs for all venous chambers ($p < 0.001$, Table 1). The Emboless reduction was superior to other chambers both at Qb200 and Qb300 ($p < 0.001$). Further, the Emboless at Qb300 still eliminated more MBs than all the other chambers at Qb200 ($p \leq 0.003$).

The proportion change (removed = improved; increased = worsened) induced by the various chambers and either Qb200 or Qb300 is shown in Figure 4. Differences in efficacy to reduce microbubble exposure to the return bloodline was also statistically analyzed in subgroups of "small", "medium", and "large" size MBs and results given in Tables 2 and 3, and Supplement Table S3.

4 | DISCUSSION

To our knowledge, the present study is the first to compare the efficacy of traditional venous chambers versus chambers incorporated in a cartridge with the aim to eliminate microbubbles of air from the return line that leads to the patient. The study showed that various numbers of MBs entered the return line of the ECC of all investigated venous chambers. In addition, the MB elimination capacity for all chambers was lowered when the blood pump speed was increased. The net increase of bubbles can be due to turbulence that disintegrates larger bubbles into smaller bubbles or by a whip and splash phenomenon when fluid forces air into the ECC.[8]

Notably, the latest developed bloodlines incorporated into a cartridge in clinical use (Artis and F6008) had the least capacity to reduce MBs. This emphasizes the important fact that the extent of MB elimination should also be addressed by companies when developing and distributing bloodlines.

The preclinical chamber Emboless had the fewest MBs in the return line and this was especially so for MBs in the larger size ranges. This was valid for Qb200 and Qb300, as well as for the Emboless Qb300 when compared with Qb200 of the other chambers. The more classic venous chambers AK98 and F5008 gave intermediate results.

TABLE 1 Paired comparison in MB elimination of all sizes of MBs

	AK98	F5008	Artis	F6008	Emboless
Qb200					
AK98	x	NS	B	B	<0.001
F5008	NS	x	B	NS	<0.001
Artis	0.001	<0.001	x	W	<0.001
F6008	0.042	NS	0.015	x	<0.001
Emboless	B	B	B	B	x
Qb300					
AK98	x	NS	B	B	<0.001
F5008	NS	x	B	B	<0.001
Artis	<0.001	<0.001	x	NS	<0.001
F6008	<0.001	<0.001	(0.060)	x	<0.001
Emboless	B	B	B	B	x

Note: The chamber in the left column is compared to those in the horizontal columns with p-values given and if the elimination of MBs was either better (B, less MBs return), worse (W, more MBs return), or no difference (NS).

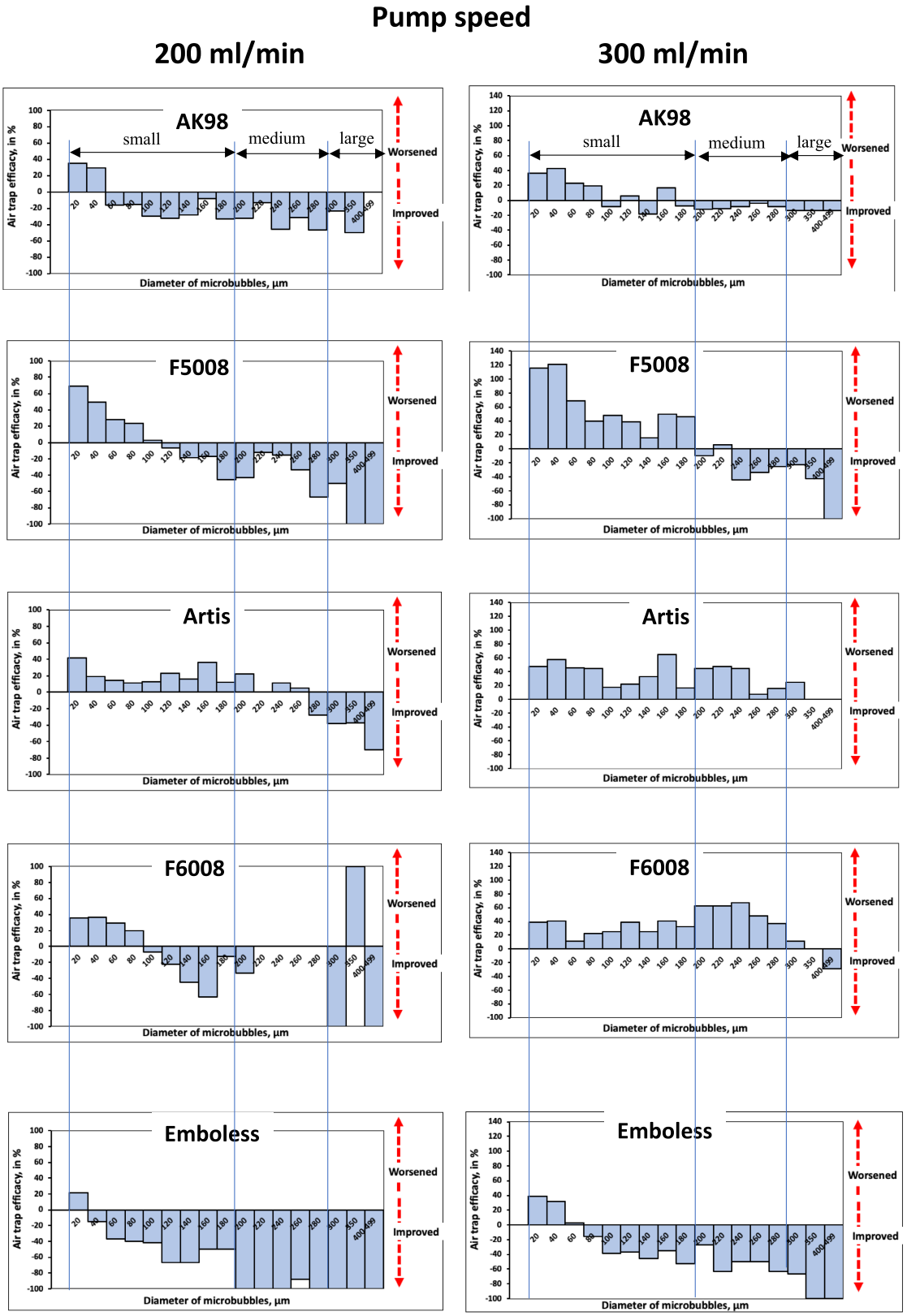

FIGURE 4 Median changes in MB count (outlet vs. inlet in %) at Qb200 (left side) or 300 ml/minute (right side) of various air traps and MB size groups (such as "20" represents data from 20 to 39 µm diameter with increasing interval with larger sizes). Inserted horizontal lines delineating the size ranges "small" (20–199 µm diameter), "medium" (200–299 µm), and "large" (300–500 µm); Efficacy scales differ between Qb200 and Qb300. [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 2 Various venous chambers and the median change (%) of their capacity to alter microbubbles in the return line versus inlet line, differentiated into small (20–199 μm diameter), medium (200–299 μm), and large (300–500 μm) sizes

Device	Qb200 Small	Qb200 Medium	Qb200 Large	Qb300 Small	Qb300 Medium	Qb300 Large
AK98	−14	−33	−25	+12	−8	−14
F5008	+12	−41	−100	+55	−20	−50
Artis	+19	+6	−56	+38	+29	+0
F6008	+0	+0	−100	+31	+54	−13
Emboless	−40	−100	−100	−20	−50	−100

Note: The blood pump speed is either 200 (Qb200) or 300 ml/minute (Qb300).

TABLE 3 Paired non-parametric comparison between various venous chambers in their capacity to change outlet versus inlet numbers of microbubbles

	Qb200 Small	Qb200 Medium	Qb200 Large	Qb300 Small	Qb300 Medium	Qb300 Large
F6008 versus						
F5008	W**	NS	W***	W***	W***	W***
Artis	B***	NS	B*	NS	NS	B**
AK98	NS	NS	NS	W***	W***	NS
Emboless	W***	W***	W***	W***	W***	W***
F5008 versus						
Artis	B**	B***	B**	W***	B***	B***
AK98	W***	NS	B***	NS	NS	B***
Emboless	W***	W**	W***	W***	W**	NS
Artis versus						
AK98	W***	W***	B***	W***	W***	NS
Emboless	W***	W***	W***	W***	W***	W***
AK98 versus						
Emboless	W***	W***	W***	W***	W***	W***

Note: The device in the upper left corner is compared with those listed below. P-values show if significant differences exist and if the outcome is better (B), worse (W), or not significantly (NS) versus the compared chamber. Size ranges given are "small" (20–199 μm diameter), "medium" (200–299 μm), and "large" (300–500 μm).

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

This shows that besides blood pump speed the shape of the venous chamber is crucial for the elimination of MBs from the bloodline. The superior effect of the Emboless is based on the 45-degree incline of blood flow from below and the shape of the venous inflow part that allows a more laminar flow. Such flow enables MBs to rise to the upper surface, aggregate, and coalesce with other MBs, before residing at the evacuation site at the top of Emboless. The flow properties of the Emboless cause no splash effects and limit turbulence as well.

Smaller bubbles are thought to collapse or to be cleared by diffusion to the alveolar space.[17] However, it is not known at what size MBs will remain in circulation and cause microthrombi. Based on autopsy studies,[10–12] MBs of all sizes stick in the vessels of the lungs while MBs below 100 μm diameter seem to pass through the pulmonary circulation and cause microembolic lesions in vital organs such as the brain and heart. Elongation of MBs may enable passage through more narrow vessels. The absorption of microbubbles is impaired as air bubbles were identified covered with a layer of fibrinogen and/or fibrin around the air bubble of the MB forming a microemboli,[10–12] and denatured proteins in the bubble blood interface further interfere with bubble dissolution.[18] A greater risk for cerebral emboli exists in patients with an open foramen ovale. In these patients, even larger and more frequent MBs entering the bloodline from the hemodialysis circuit may transit to the left heart and the arterial side. Such exposure may explain the fact that HD patients suffer from pulmonary damage, cerebral microinfarctions, dementia, and myocardial stunning; these conditions are more common for HD than for patients on peritoneal dialysis who are not exposed to MBs from an ECC.[19] A shorter life expectancy was noted for HD patients dialyzed with higher blood pump speed and shorter dialysis time,[20,21] albeit other factors may also be

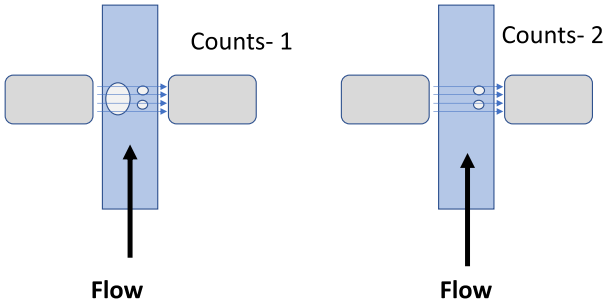

FIGURE 5 The figure shows limitation in the detection abilities of ultrasound. In the left a large bubble will shadow two smaller bubbles and the results will be one larger count only. On the right figure, such shadowing effect is not present. [Color figure can be viewed at wileyonlinelibrary.com]

important. Such patients would be more exposed to microemboli from the ECC.[6,7,9,19]

We recommend that companies report the MB exposure within their bloodline systems at Qb200 and Qb300. It is important that the settings do not have a too large exposure (too many MBs produced in the system) that results in shedding of bubbles and false low counts (Figure 5).

A limitation of the study design is that the perfusion model with one transducer on the inlet side of the venous chamber and another on the outlet side will result in a delay in the peak of MB counts from the inlet until the remaining MBs appear at the outlet. More delay exists in a larger chamber and with lower blood pump speed. This may result in positive or negative outcome measures (ratio of outbound vs. inbound MBs of a specific size) for especially large-sized MBs of which fewer counts appear within 6 min. This effect can be minimized by starting and ending the investigation having a low MB exposure. This is done by avoiding knocking the dialyzer during the first and last 30 s of the exposure. For more accurate data time, adjustments may be made. In the present study, the conditions were set equal for all venous chambers.

Although none of the chambers removed all MBs, the present study clearly showed significant differences in elimination. Removal of larger MBs may be more crucial in one regard as larger vessels in the lungs can get obstructed and cause pulmonary hypertension and perfusion reduction. However, we do not know to what extent larger MBs may be disrupted and disintegrated into smaller MBs. Smaller MBs to a large extent may pass through the pulmonary vessels and end up in crucial areas of organs on the side of the arterial circuit, such as the brain and heart. It is not clear how fast and how extensive clots are formed around the MBs. The aim should be that MBs are eliminated as much as practical from entering any organ of the patient.[22] This is to prevent from chronic tissue damage[11,12] and in the worst case also from acute life-threatening MBs such as in the sinus node.

Our data provide a view of the technical level (in Medical Device Regulation: State of the art) of safety performance according to the dialysis systems on the present market and in clinical use.[13] The present study shows that newer systems in clinical use do not perform better than earlier systems. The data of the newly developed venous chamber Emboless indicate that the technical level of reduction according to micro air infusion can be further improved. A follow-up in vivo clinical test is ongoing to verify this new performance.

As the field of MBs has not received much attention over the years, we are aware that manufacturers have been reluctant to adopt bubble traps that were presented to them. Even if such a chamber would fit their device, it would need some administrative work, while in some devices, modifications on the design of the dialysis monitors would also be needed. In future dialysis developments, these are issues that are being addressed.[23]

4.1 | Conclusion

The choice of venous chamber and Qb is important to limit exposure of microbubbles that enter the patient and may cause microemboli in lung, brain, and heart. The results from the present study indicate that the different flow characteristics of the venous chamber and the Qb are important factors to limit exposure of MB to the return bloodline. The Emboless chamber reduced MBs more effective than those chambers in clinical use investigated.

AUTHOR CONTRIBUTIONS

All authors contributed equally to concept/design, data analysis/interpretation, critical revision of the article and approval of the article. Data collection was done by PJ and BS, drafting the article was done by PJ, statistical analyses was done by BS, and funding was secured by all authors.

CONFLICT OF INTEREST

All four authors are researchers within the frame of Umea University, and in the area of development of Medical Devices. To clarify the value of a patented venous chamber Emboless, a company was initiated (Embody AB). To decide if it may be worth the investment to perform a clinical study of Emboless the present comparative, in vitro study, was made. All authors are the sole stockholders of the Embody AB company.

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REFERENCES

1. Jonsson P, Lindmark L, Axelsson J, Karlsson L, Lundberg L, Stegmayr B. Formation of blood foam in the air trap during hemodialysis due to insufficient automatic priming of dialyzers. Artif Organs. 2018;42:533–9.

2. Wagner S, Rode C, Wojke R, Canaud B. Observation of microbubbles during standard dialysis treatments. Clin Kidney J. 2015;8:400–4.
3. Jonsson P. Safety and biological aspects of present techniques of haemodialysis [Umeå University medical dissertations]. Print & Media, Umea, Sweden: Umea University; 2006.
4. Polaschegg HD. Hemodialysis machine air detectors need not detect microbubbles. Artif Organs. 2007;31:911–2. author reply 3-4.
5. Polaschegg HD, Levin N. Hemodialysis machines and monitors. In: Winchester J, Koch R, Lindsay R, Ronco C, Horl W, editors. Replacement of renal function by dialysis. 5th ed. Dordrecht: Kluwer Academic Publishers; 2004. p. 323–447.
6. Jonsson P, Karlsson L, Forsberg U, Gref M, Stegmayr C, Stegmayr B. Air bubbles pass the security system of the dialysis device without alarming. Artif Organs. 2007;31:132–9.
7. Stegmayr B, Forsberg U, Jonsson P, Stegmayr C. The sensor in the venous chamber does not prevent passage of air bubbles during hemodialysis. Artif Organs. 2007;31:162–6.
8. Stegmayr CJ, Jonsson P, Forsberg U, Stegmayr BG. Development of air micro bubbles in the venous outlet line: an in vitro analysis of various air traps used for hemodialysis. Artif Organs. 2007;31:483–8.
9. Forsberg U, Jonsson P, Stegmayr C, Jonsson F, Nilsson B, Nilsson Ekdahl K, et al. A high blood level in the venous chamber and a wet-stored dialyzer help to reduce exposure for microemboli during hemodialysis. Hemodial Int. 2013;17:612–7.
10. Stegmayr B, Brannstrom T, Forsberg U, Jonson P, Stegmayr C, Hultdin J. Microbubbles of air may occur in the organs of hemodialysis patients. ASAIO J. 2012;58:177–9.
11. Forsberg U, Jonsson P, Stegmayr B. Air contamination during medical treatment results in deposits of microemboli in the lungs: an autopsy study. Int J Artif Organs. 2019;42:477–81.
12. Forsberg U, Jonsson P, Stegmayr B. Microemboli induced by air bubbles may be deposited in organs as a consequence of contamination during medical care. Clin Kidney J. 2022;15:sfac217.
13. European Parliament. REGULATION (EU) 2017/745 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC. In: Parliament E, ed. Official Journal of the European Parliament. Brussels: EU Commission; 2017. https://www.medical-device-regulation.eu/download-mdr/
14. Stegmayr C, Jonsson P, Forsberg U, Stegmayr B. Hemodialysis dialyzers contribute to contamination of air microemboli that bypass the alarm system in the air trap. Int J Artif Organs. 2008;31:317–22.
15. Hecking M, Bieber BA, Ethier J, Kautzky-Willer A, Sunder-Plassmann G, Säemann MD, et al. Sex-specific differences in hemodialysis prevalence and practices and the male-to-female mortality rate: the dialysis outcomes and practice patterns study (DOPPS). PLoS Med. 2014;11:e1001750.
16. Forsberg U, Jonsson P, Stegmayr C, Stegmayr B. A high blood level in the air trap reduces microemboli during hemodialysis. Artif Organs. 2012;36:525–9.
17. Polaschegg H-D, Levin N. Hemodialysis machines and monitors. Air embolism. In: Hörl W, Koch K, Lindsay R, Ronco C, Winchester J, editors. Replacement of renal function by dialysis. 5th ed. London, Great Britain: Kluwer Academic Publishers; 2004. p. 334–41.
18. Barak M, Nakhoul F, Katz Y. Pathophysiology and clinical implications of microbubbles during hemodialysis. Semin Dial. 2008;21:232–8.
19. Stegmayr B. Air contamination during hemodialysis should be minimized. Hemodial Int. 2017;21:168–72.
20. Charra B, Chazot C, Jean G, Hurot JM, Vanel T, Terrat JC, et al. Long 3 ×8 hr dialysis: the Tassin experience. Nefrologia i Dializoterapia Polska. 2006;10:141–6.
21. Matsuda K, Fissell R, Ash S, Stegmayr B. Long-term survival for hemodialysis patients differ in Japan versus Europe and the USA. What might the reasons Be? Artif Organs. 2018;42:1112–8.
22. ISO 14971:2019. Medical devices – Application of risk management to medical devices (ISO 14971:2019). Brussels: CEN-CENELEC; 2019.
23. Groth T, Stegmayr BG, Ash SR, Kuchinka J, Wieringa FP, Fissell WH, et al. Wearable and implantable artificial kidney devices for end-stage kidney disease treatment-current status and review. Artif Organs. 2022. https://doi.org/10.1111/aor.14396

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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