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Thrombus Formation in Centrifugal Pumps

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Abstract

Three centrifugal flow pumps; the Biomedicus BP80, the Sarns Delphin and the Aries Lifestream 2100, were evaluated in vitro to determine each pump's individual tendencies for thrombus formation. Thrombogenic surfaces in the circuit were minimized by using heparin coated tubing and connectors. The centrifugal pumps, which were not heparin bonded, were placed in line in a circuit which consisted of a venous reservoir, a heat exchanger and a centrifugal pump.

One trial was performed for each of the three pumps by priming the circuits with approximately 500 ml of fresh heparinized bovine plasma. Protamine sulfate was titrated in slowly to decrease the activated clotting time (ACT) from an initial level of >600 seconds back to baseline. The thrombus formation was documented on videotape using a strobe lamp flashed at a frequency compatible with the pump's rpm.

Thrombus formation was observed in each of the centrifugal pumps we evaluated. We have determined that the centrifugal pump is a potential source of thrombus formation and it may result in an increased morbidity or mortality for the patient when used for cardiopulmonary bypass or ventricular assist without adequate systemic heparinization.

Introduction

This experiment was designed to determine if non-heparin treated centrifugal pumps are an origin for thrombus formation, and to determine if all current centrifugal pumps on the market possess the same risk of thrombus formation.

Clot formation has been found to occur in the centrifugal pump in the areas of the pump with the highest temperatures, the lowest shear forces and lowest velocity of flow. (1) In the centrifugal pump, this is primarily in the areas of the pump inlet and the bearing housing. In the past this thrombus formation has been felt to be clinically insignificant and related more to the connectors and areas of stasis within the circuit rather than to the pump itself. For this reason it is not unusual to find centrifugal pumps being used without systemic heparinization in extracorporeal circuits for left ventricular assist (1,8,9), aneurysm repair (9) and liver transplantation. (2,3)

Previous studies have been inconclusive concerning the safety of the centrifugal pump without systemic heparinization. For example, in a blind comparison study using mongrel dogs, van der Hulst found no difference in circuits that were heparin coated, versus the non-heparin coated circuits, using a Sarns centrifugal pump. Clot formation was equally distributed between both the coated and the uncoated groups and was found to occur at the axis of the pump head as well as at the catheter tip. In addition, at autopsy, 4-5 mm emboli were found in the dogs' pulmonary arteries. (3) Steinhorn, et al., noted clot formation in six out of seven circuits used for neonatal ECMO. The neonates in this study were anticoagulated to a mean partial thromboplastin time (PTT) of 57.4 seconds. No thrombus formation could be identified in the Biomedicus pump in any of these cases. (4)

On the other hand, Yozu, et al., perfused five bovine models with an ACT of twice normal and found the build up of an "amorphous type of material" under the "impeller and adjacent baffle" of a Biomedicus pump requiring a frequent changing of the pumps. (5) In another study, Bernstein, et al., found clot formation around the bearing seals and found occasional renal thrombi while using a new experimental centrifugal pump. (6)

Using mongrel dogs, Dixon, et al., noted thrombus formation around the center shaft of a Biomedicus Bio-Pump used for left ventricular assist. Perfused without systemic heparinization, the dogs were noted to have small renal infarcts at autopsy. The authors, however, postulated that the clots were generated proximal to the pump, in the tubing and

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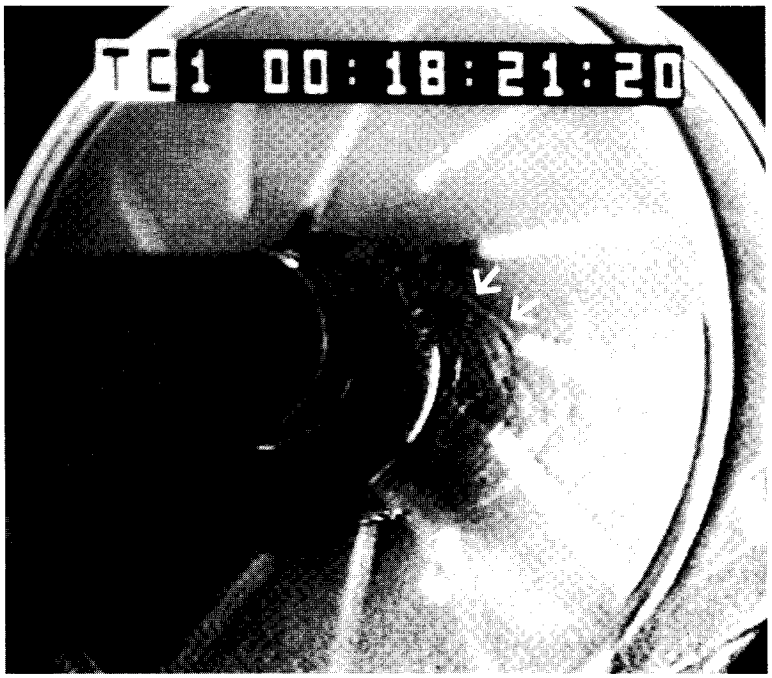

Figure 1
In the Sarns Delphin, 10.5 minutes after reaching baseline ACT, a thin strand of fibrin-type material (at arrows) is seen extending from the pump inlet side of a long vane to the shorter vane below it.

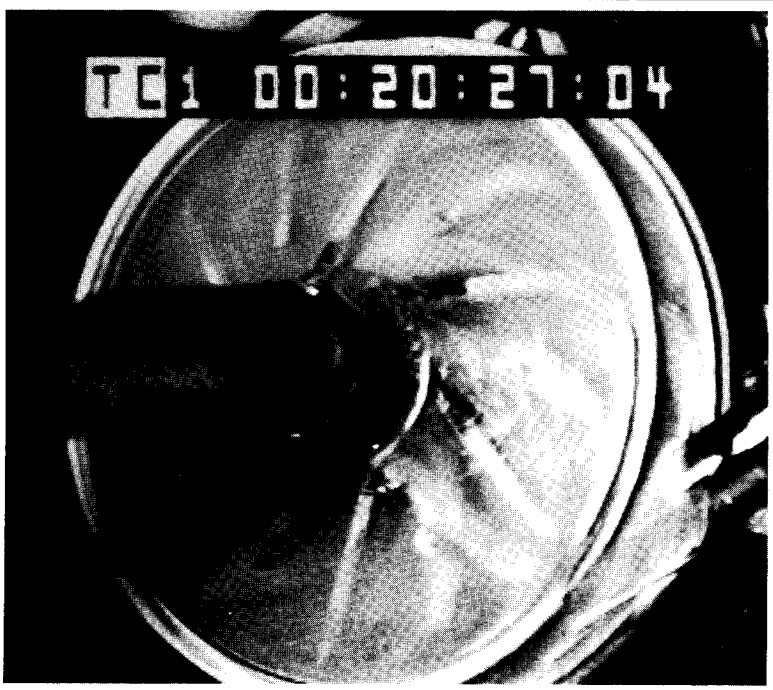

Figure 2
127 seconds after the first evidence of thrombus formation, massive cotton-like thrombi prevent any further forward flow in the Sarns Delphin. A string of thrombus may be seen extending back from the pump for several inches.

connectors, and broke free of the pump's vortex when they reached sufficient mass. (7) In a three part study with the Bio-Pump, Dixon and Magovern found no clot formation in dogs heparinized to 150-175 seconds while on cardiopulmonary bypass. They also found no clot formation in dogs on left ventricular assist without systemic heparinization. In the last part of the study, again using left ventricular assist, a sheep model was found to have a large renal infarct at autopsy. Examination of the pump showed clot formation around the center shaft of the Biomedicus pump. (8)

In another study using a sheep model, Magovern, et al., found that no anticoagulation was needed when a Biomedicus Bio-Pump was used for periods up to two weeks at 2000-3000 rpm. However, at 10-14 days thrombus formation in the bearing housing resulted in systemic embolization. (1)

Finally, in a study of seven patients maintained with ACTs of less than 200 seconds while using ventricular assist devices, at intervals of up to 96.5 hours, Mills and associates found centrifugal pumps to be athrombogenic. (9)

Our video observation demonstrated in vitro evidence that thrombus formation may occur in all currently available centrifugal pumps following heparin neutralization.

Materials and Methods

Three heparin coated circuits, identical except for the centrifugal pump and each consisting of a centrifugal pump, a heat exchanger and a venous reservoir, were created. The circuit was connected as follows: a centrifugal pump — either a Sarns Delphin[a], a Biomedicus Bio-Pump BP-80[b] or an Aries Lifestream 2000[c] — was connected in-line to a SciMed Heat Exchanger[d], which returned the plasma back to a Bentley BMR 1800[e] venous reservoir and then back to the centrifugal pump. All components, except for the centrifugal pumps, were coated with Bentley Duroflo II[e] to minimize surface activation of the coagulation cascade within the circuit.

To permit easy visualization of the fibrin and

a Sarns 3M Healthcare, Ann Arbor MI 48013
b Biomedicus, Eden Prairie MN 55344
c Aries Medical Inc., Chelmsford MA 01824
d Sci-Med Life Systems Inc., Minneapolis MN 55441
e Bentley Laboratories, Irvine CA 92714

the thrombus formation we used bovine plasma. Fresh blood, heparinized with 12 units/ml beef lung heparin was collected from a humanely sacrificed cow in compliance with the National Institutes of Health (NIH) "Guide for the Care and Use of Laboratory Animals" (NIH publication No. 85-23, revised 1985). The bovine blood was spun into platelet rich plasma (PRP) using the sequester mode of a Haemonetics Cell Saver[f]. Each circuit was primed with approximately 500cc of platelet rich plasma. Fibrinogen levels and platelet counts were drawn from the PRP to insure that an adequate and consistent substrate was available for fibrin formation. The platelet count was 99,000 mm^3 and the fibrinogen level was 392 mg/dl. Activated clotting times obtained from a Hemochron ACT analyzer[g] were greater than 1000 seconds at the start of the study. The temperature of the plasma was kept at 37 degrees Celsius using a Sarns dual cooler/heater[e]. The ACTs were lowered to a baseline value of 108-111 seconds by titrating in protamine sulfate.

Each pump was maintained at 2000 rpm and flow was restricted to 3.0 liters/minute by using a partially occlusive clamp on the pump outlet tubing. Inlet and outlet pump pressures were not monitored. It is possible that pressure differences between the pumps might have caused differences in temperature to occur. We do not know if this happened in our study, or if the temperature differences were significant enough to alter the generation of thrombus.

Flow was measured in all three circuits with Sarns' doppler flow probe. Fibrin and thrombus were documented on VHS videotape using a Panasonic 200 CLE camcorder[h]. To stop the geometry of the pump we set our strobe lamp to a flashing frequency of 4000 cycles per minute. Thrombus formation was defined as the gross appearance of white fibrin threads and platelet aggregates.

Results

We have demonstrated gross thrombus formation in all three of the centrifugal pumps that we tested. In each case, thrombus formation was observed within 16 minutes of the ACT reaching a

f Haemonetics Inc., Braintree MA
g International Technidyne Corp., Edison NJ 08820
h Matshuhita Communication Corp., Japan

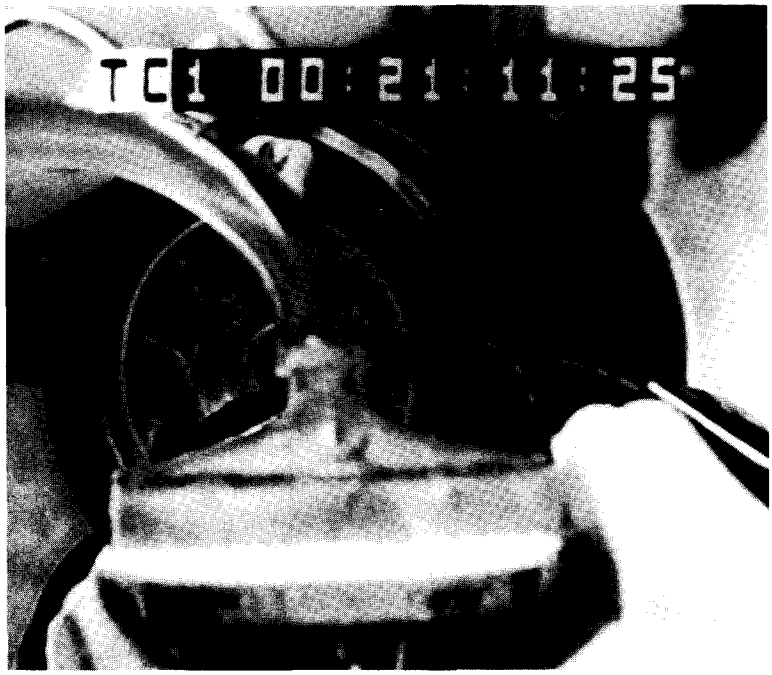

Figure 3
This lateral view of the Sarns Delphin shows a large clot in the pump inlet.

Figure 4
In this view of the Aries Lifestream, taken 22 seconds after thrombus was observed, a strand of thrombus (see arrows) is observed extending between two vanes. The loss of clear definition on the proximal, superior surface of the long vane is due to thrombi adhering to it.

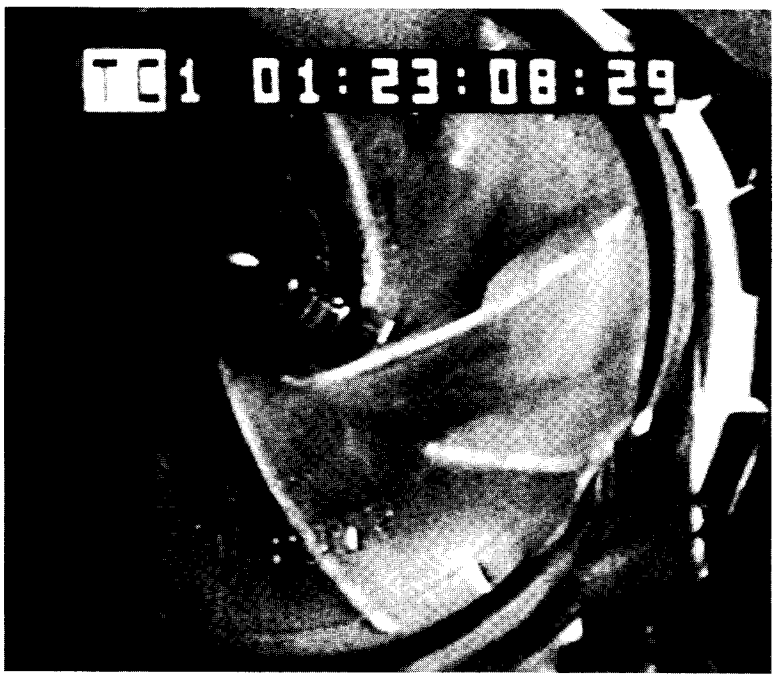

Figure 5
At 143 seconds, thrombi are seen on both the long and short vanes of the Aries pump with especially heavy thrombus formation occurring between the distal long vane and the short vane below it.

Figure 6
This view of the Aries Lifestream, taken 59 seconds before flow was lost, shows the massive clot formation within the pump.

baseline of 108 seconds. Additionally, forward flow ceased in each of our models within 5 minutes of the first evidence of thrombus formation.

The Sarns Delphin demonstrated the first evidence of fibrin formation at time counter TC1 00:18:00, 10.5 minutes after reaching baseline ACT. Figure 1 shows a wisp of a fibrin type material attached to the innermost portion of the inferior surface of a long vane and flowing outward and inferiorly over the small vane below it. In Figure 2 the massive white thrombus formation can be readily observed attached to the innermost portion of the vanes at the pump inlet. From this central point of attachment, the thrombus can be seen fanning outward and engulfing the shorter vanes. In addition, a long string of fibrin and platelet mesh can be observed attached at the pump inlet extending back for several inches in the pump vortex. Approximately 2.5 minutes after the appearance of thrombus, we were unable to detect forward flow in the pump. The videotape graphically demonstrated that the thrombus formation was greatest on the inferior surfaces of the large vanes and the superior surfaces of the smaller vanes. Figure 3 shows the lateral aspect of the Sarns pump with a large clot in the pump inlet.

The Aries Lifestream 2000 developed fibrin formation 12.5 minutes after reaching a baseline ACT of 109 seconds. At time marker TC1 01:21:45 the first fibrin formation was observed on videotape. Figure 4 shows a fibrin thread attached to the mid superior portion of a long vane and attached to the inferior surface of the short vane above it. Figure 5 shows that thrombus has formed on the superior surfaces of both the long and the short vanes. Figure 6 shows the pump engulfed in fluffy appearing thrombus shortly before the loss of forward flow. At TC1 1:26:10, 4.5 minutes after the initial thrombus was observed we could not demonstrate any more forward flow. A large clot that formed at the pump inlet was readily observed in the videotape but, unfortunately, did not lend itself to still photography.

Thrombus formation in the Biomedicus was first visualized 16 minutes after the ACT was reduced to a baseline of 110 seconds. At TC1 01:28:50 small thrombi, which looked much like small air emboli, began to swirl in the vortex at the pump inlet. Figure 7 demonstrates how the thrombi spread within minutes to the outer edges of the cones where they began to catch on the cone spacers. In Figure 8, thrombus can be seen freely

spinning within the pump as well as attached to the cone spacers. Three minutes after seeing the first thrombus, we were unable to demonstrate forward flow in the Biomedicus. Figure 9, taken after flow had stopped, shows the jelled center of the Bio-pump and the thrombus wrapped around the cone spacers. The underside of the Bio-Pump demonstrated a small thrombus trapped at the edge between the magnet and the housing. The depth of the Biomedicus cone and the turbidity of the plasma combined to make it difficult to show the detail shown in the other pump photographs.

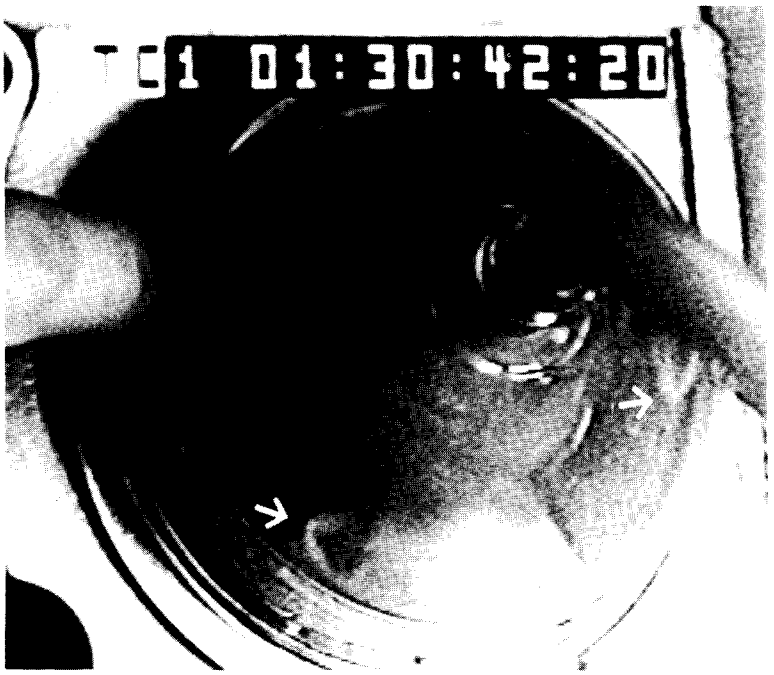

Figure 7
This view of the Biomedicus BP-80, taken 2.5 minutes after the first thrombus formation was observed, shows thrombi caught on the cone spacers (single arrows). A large free-spinning thrombus is pointed out at the double arrows.

Discussion

Our model demonstrates that thrombus formation and embolization are a realistic threat to patients undergoing extracorporeal circulation without adequate heparinization. Although Magovern, et al., and Dixon, et al., have endorsed heparinless ventricular assist (1,8), clot formation, however significant, did occur in their studies. (1,7,8) They hypothesize that the reason major coagulation problems are unnoticed in vivo is because, even though the platelet and other coagulation factors are activated, the perfused organism may be in a state of "controlled fibrinolysis", where the patient's fibrinolytic system can keep pace with the fibrin and thrombus formation. (1,8)

Our study, separated from an intact fibrinolytic system, showed major thrombus formation occuring quickly after the ACT reached baseline. Whether the results of this study can be applied to the in vivo use of centrifugal pumps is uncertain. It does, however, demonstrate that centrifuagl pumps are not immune to thrombus formation. The decision to use heparinless bypass, or to totally reverse heparinization, should be made with the possible consequences kept in mind.

Conclusion

A search of the literature reveals conflicting reports regarding the safety of using centrifugal pumps for purposes of ventricular assist without systemic heparinization. We have documented evidence that thrombus formation may occur in centrifugal pumps in the absence of heparinization. Additionally, we have shown it will occur in all non-heparin treated centrifugal pumps currently being used in clinical practice. Finally, we demonstrated that embolization of thrombi might be possible since forward flow continues for several minutes after the first evidence of thrombus formation.

This study presented an in vitro observation of thrombus formation only. The potential risk of in vivo thrombus formation remains unanswered. We recommend that the practice of using centrifugal pumps for heparinless bypass be reevaluated and strong consideration be given to using some anticoagulation, perhaps to an ACT of 180 to 200 seconds, for the duration of the circulatory assist.

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Figure 8
In this view of the Biomedicus, the thrombus on the spacers is visualized. The lighter appearance of the pump center, as compared to Figure 7, is due to the accumulation of many tiny thrombi awirling between the cones in the pump inlet.

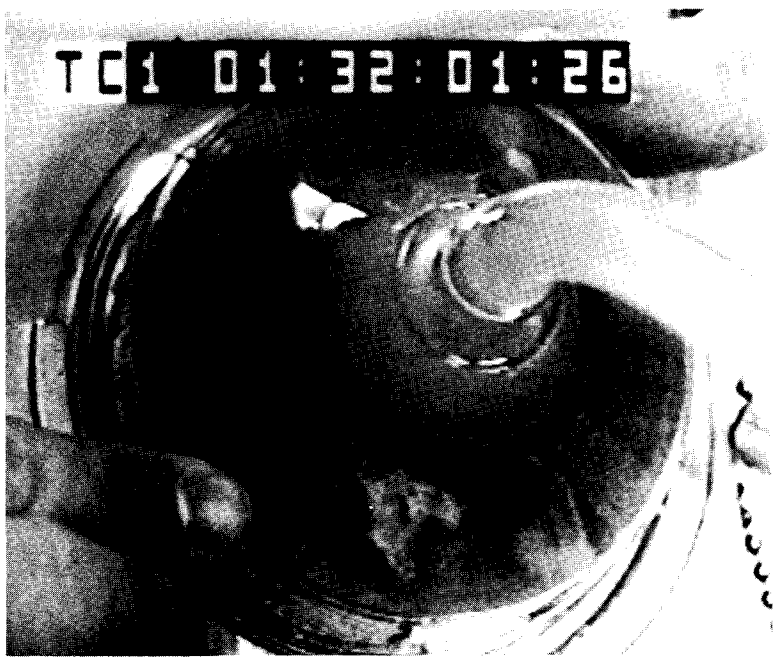

Figure 9
In this view of the BP-80, taken after the cessation of forward flow, numerous thrombi are easily seen. The jellied inlet of the Bio-Pump is more easily appreciated in this view.

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