Excerpta Medica

The American Journal of Surgery®

The American Journal of Surgery 188 (2004) 722–727
Scientific paper

A prospective randomized trial demonstrating valved implantable ports have fewer complications and lower overall cost than nonvalved implantable ports

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Manuscript received July 20, 2004; revised manuscript August 7, 2004

Presented at the 56th Annual Meeting of the Southwestern Surgical Congress, Monterey, California, April 18–21, 2004

Abstract

Background: The purpose of the current study was to evaluate whether a totally implanted valved subcutaneous port system would have fewer complications as compared to a standard nonvalved port.

Methods: Study subjects requiring port placement were randomized to receive a valved port (PASV; Boston Scientific, Natick, MA) or a nonvalved port (BardPort; Bard Accesss Systems, Salt Lake City, UT). Each port was placed with standard operative technique. Difficulty with blood return, excess time spent accessing the port, and required interventions were reported over the initial 180 days of port usage.

Results: Seventy-three patients were randomized to receive either a valved port (n = 37) or a nonvalved port (n = 36). No major complications were identified from port placement, and there were no differences in rates of infection between the 2 ports. A reported inability to withdraw blood was noted in the valved port group on 21 of 364 (5.8%) port accessions and in the nonvalved port group on 37 of 341 (11%) accessions ($P = 0.02$). Significantly more total time was spent ensuring adequate blood draw from nonvalved ports as opposed to valved ports (750 minutes vs. 1545 minutes, respectively) ($P < 0.03$).

Conclusions: This study revealed that the PASV valved port is associated with significantly fewer instances of poor blood return and less nursing access time, indicating that a port with a PASV valve may be superior to a nonvalved device.

Keywords: Long-term central venous access; Central line complications; Implantable ports; Catheter tip thrombosis

Reliable central venous access is necessary for the treatment of patients who require chemotherapy, prolonged antibiotic therapy, parental nutrition, and frequent blood draws [1]. Totally implantable venous access devices have been developed and represent a technologically superior solution for long-term access [2]. Several postimplantation complications relating to these devices continue to occur, including catheter occlusion, infection, air embolus, and venous thrombosis. Catheter tip occlusion and clotting has been a particularly common complication resulting in the estimated cost to the US healthcare system of more than $1 billion per year [3,4].

There have been few reported clinical studies describing initial port access failures. Catheter tip occlusion from thrombus, mechanical kinking, or the catheter tip abutting the wall of the vein are all described as reasons for blood draw failures [5]. When blood initially cannot be drawn from the port, additional procedures become necessary, resulting in increased nursing time, additional studies such as chest radiography, and thrombolytic medications such as tissue plasminogen activator (t-PA).

Catheter tip thrombosis has been shown to occur in up to 28% of patients using totally implanted ports [6]. This thrombosis may be due to the reflux of blood into the distal tip of the catheter when the access needle is removed or with increased intrathoracic pressures (i.e., valsalva). Tensile pressure on the port diaphragm with needle removal produces a quantifiable negative pressure, which causes the influx of blood through the tip. Laboratory analysis has shown that this influx can cause a static column of blood up to 5 mm in length from the catheter tip. The column of

Supported by a grant from Boston Scientific/Meditech

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0002-9610/04/$ – see front matter
doi:10.1016/j.amjsurg.2004.08.041

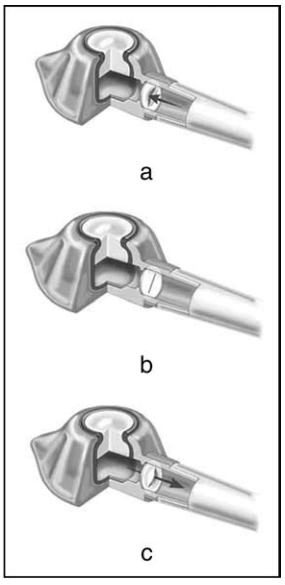

Fig. 1. Diagrams demonstrating the PASV valve and its position relative to the port usage. (**a**) The valve allows blood to enter the reservoir with the pressure created by an aspiration needle. (**b**) The valve remains closed during needle removal and when the port is not being used. (**c**) The valve allows infusion under minimal pressure.

blood then evolves into a thrombus. Strategies to minimize blood reflux in the catheter include the placement of a pressure activated safety valve (PASV; Boston Scientific, Natick, MA) close to the port reservoir. The PASV valve is designed to automatically close after infusion, aspiration, or upon accidental disconnection. The valve opens easily for normal infusion, but the increased pressure required to open the valve for aspiration automatically resists backflow during normal intrathoracic pressure fluctuations (see Fig. 1).

A prior clinical study using valved peripherally inserted central catheter (PICC) lines compared with nonvalved PICC lines demonstrated a decreased rate of catheter clotting [7]. The purpose of the current study was to evaluate whether a valved subcutaneous port system would have fewer associated complications as compared to a standard nonvalved port and whether the fewer complications demonstrated a cost-saving benefit.

Methods

Patients

This prospective randomized trial was conducted with the approval of the institutional review board at Baylor University Medical Center. Eligible study subjects were 18 years or older who required long-term venous access for chemotherapy, blood draws, or total parenteral nutrition. Patients were excluded if they had a central venous access port within the preceding 6 months or if they were fully anticoagulated for any reason. Informed consent was obtained from each patient enrolled in the study.

Catheters, implantation, and catheter maintenance

Patients were randomly assigned to undergo implantation of a 9.6-F single-lumen PASV port catheter or a same sized control nonvalved BardPort (Bard Access Systems, Salt Lake City, UT). Catheter placement was performed by standard technique into either the subclavian or internal jugular vein. Appropriate placement was confirmed with intraoperative fluoroscopy and documented by postoperative chest radiograph. Initial port function was insured by intraoperative access prior to skin closure.

All infusions through the catheter were administered according to the appropriate manufacturer's recommendations. For the valved port group, catheters were flushed after each accession with 10 mL of normal saline, while the nonvalved group used 10 mL of heparinized saline. Patients who exhibited signs or symptoms of catheter-related infection were treated appropriately. A catheter occlusion was suspected when the infusion nurse could not withdraw blood with initial aspiration. Initial maneuvers included catheter needle manipulation and flushing, as well as patient repositioning. If this proved unsuccessful, additional diagnostic maneuvers were performed, including chest radiography and/or physician consultation. Suspected catheter occlusion was treated with t-PA per standard hospital protocol.

Data collection and analysis

Patients were followed for the purposes of this study for 180 days or until port removal. Patient interviews and prospectively maintained nursing records were used to evaluate adequacy of port function. Antibiotic treatment, difficulty drawing blood or infusing through the port (including number of events), need for further studies (chest radiography, duplex ultrasonography, or contrast studies), and hospitalizations related to the port were recorded. Inability to withdraw blood was defined as not being able to withdraw at least 5 mL of blood on initial access. The use of thrombolytics to re-establish catheter patency also was recorded. Time to access the port was prospectively documented by nursing personnel at each accession.

A cost analysis was performed comparing the port types. Fixed costs included the cost of the ports ($397 for the BardPort vs. $535 for the PASV port), cost of initial access infusion (BardPort requires heparinized saline, $8.50), cost of post-access infusion ($12.60 using heparinized saline for the BardPort vs. $7.45 using normal saline for the PASV port), nursing access time cost ($30 per hour), and infusion room time ($75 per hour). Upon failure to withdraw blood after these initial maneuvers, additional costs included chest x-ray ($48 per film + $12 per interpretation), cost of thrombolytic therapy ($371 for t-PA), and t-PA infusion ($91 nursing charge + $18 per access kit). Fixed costs that were the same between the port groups included implantation costs, cost of catheter infection, and venous thrombosis and were not included in the analysis. Cost comparisons were

Table 1
Baseline demographic data

	PASV (n = 37)	BardPort (n = 36)	*P*
Gender, n (%)			
Female	33 (89.2)	29 (80.6)	0.92
Male	4 (10.8)	7 (19.4)	0.57
Median age, yr (range)	54 (23–83)	54.6 (25–76)	0.99
Malignancy, n (%)			
Breast	23 (62.2)	21 (58.3)	0.86
Gastrointestinal	5 (13.5)	5 (13.8)	1.0
Hematologic	2 (5.4)	5 (13.8)	0.43
Gynecologic	4 (10.8)	1 (2.7)	0.36
Genitourinary	2 (5.4)	2 (5.5)	1.0
Lung	1 (2.7)	1 (2.7)	1.0
Skin	0	1 (2.7)	0.99

made between the 2 experimental groups based on differences in device cost, maintenance, t-PA usage, and nursing access time. The total cost in each experimental group was then divided by the number of patients in each group to give an average cost per patient. This per-patient cost was compared between the 2 groups.

Demographic and disease characteristics were summarized for all patients and are reported using descriptive statistics. Baseline incidence of demographic variables, device complications, and additional time spent caring for catheters were compared between experimental and control groups using 2-sample asymptotic *t* tests for proportions. Statistical significance was defined as $P < 0.05$. All statistical calculations were performed using Stat View 5.0 (SAS Software, Cary, NC).

Results

Ports were successfully placed in all 73 patients and comprise the study population. Using random assignment, 37 patients were implanted with a valved (PASV) port and 36 with a nonvalved (BardPort) port. Baseline demographic data are shown in Table 1. All patients were being treated for an underlying malignancy. Data for 180 days postimplantation are complete for all patients. No significant differences in demographic data were identified between the 2 groups.

Major complications during this time period are shown in Table 2. Again, no significant differences in major complications were observed between the 2 groups. One patient in the nonvalved port group was found to have a fractured catheter at the connection to the port, which was documented by a contrast study. The port was subsequently removed. One patient in each group had an internal jugular venous thrombosis, both of which were treated with anticoagulation without port removal. Two patients in the valved group were treated for cellulitis surrounding the port pocket, which occurred before the first accession of the port.

Table 2
Major complications during the first 180 days postimplantation

	PASV (n = 37)	Bardport (n = 36)	*P*
Port-site cellulitis, n	2 (7.4%)	0	0.5
Catheter sepsis, n	1 (2.7%)	1 (2.8%)	1.0
Catheter leakage, n	0	1 (2.8%)	1.0
Venous thrombosis, n	1 (2.7%)	1 (2.8%)	1.0

One patient in each group was hospitalized for catheter-related sepsis. Both patients received antibiotics, and their ports were removed. Both patients recovered uneventfully.

The ability to withdraw blood was recorded each time a port was accessed. Port access totals and difficulties withdrawing blood over the 180-day period are shown in Table 3. Valved ports were associated with significantly fewer difficulties drawing blood as compared to nonvalved ports (5.8% vs. 11%, $P = 0.02$). Additionally, vavled ports (3.0%) versus nonvalved ports (6.1%) had fewer reported access difficulties that required additional access time (>30 minutess, $P = 0.05$). Additional time spent assessing and treating inadequate blood draw in the nonvalved port group was twice that found in the valved port group (750 vs. 1545 minutes, $P < 0.03$). There was also a trend toward less use of t-PA in the valved port group, although this did not reach statistical significance.

The results of the cost analysis are shown on Table 4. The per unit acquisition cost of the PASV port is $138 more than the BardPort. However, the average increase in the maintenance infusion costs, additional nursing and room time required to obtain proper blood draw in nonvalved group added an additional $193 cost per unit to that group, compared to adding only $108 in additional cost per unit to the valved port group. Additionally, the costs associated with a failure to achieve blood return included the routine use of chest radiography to assess for possible catheter separation, a medical oncologist evaluation, and t-PA infusion. These costs associated with the failure to achieve

Table 3
Port access during 180 days postimplantation

	PASV (n = 37)	BardPort (n = 36)	*P*
Total accessions, n	364	341	0.89
Difficulty withdrawing blood occurrences*	11 (3.0%)	21 (6.1%)	0.05
Patients, n with >2 episodes of inability to draw blood	3 (8.1%)	7 (19.4%)	0.18
Inability to withdraw blood occurrences, n	21 (5.8%)	37 (11%)	0.02
t-PA use, n	16 (4.4%)	23 (6.7%)	0.20
Total time to ensure port patency, min	750	1545	<0.03

* Requiring extra flushing or catheter manipulation resulting in ≥30 minutes nurse infusion time.

Table 4
Cost analysis between the PASV and the BardPort

	PASV Port		BardPort	
	Calculation	Total	Calculation	Total
Port insertion costs				
Port acquisition	$535 × 37	$19,795	$397 × 36	$14,292
Heparin flush	N/A	—	$8.50 × 36	$306
Maintenance costs				
Saline flush	$7.45 × 364 accessions	$2,712	N/A	—
Heparinized flush	N/A	—	$12.60 × 341 accessions	$4,297
Nursing access time	12.5 h × $30	$375	25.75 h × $30	$773
Infusion room time	12.5 h × $75	$938	25.75 h × $75	$1,931
Failure to withdraw costs				
Evaluation				
Chest x-ray	21 events × $60	$1,260	37 events × $60	$2,220
Infusion room delay	1 h × $75/h × 21 events	$1,575	1 h × $75/h × 37 events	$2,775
Physician time	10 min × $200/h × 21 events	$700	10 min × $200/h × 37 events	$1,233
Correction				
t-PA usage	$371 × 16 events	$5,936	$371 × 23 events	$8,533
Nurse administration time	$91 × 16 events	$1,456	$91 × 23 events	$2,093
Access kits	$18 × 16 events	$288	$18 × 23 events	$414
Total costs	$35,035		$38,867	
Cost/unit summary				
Port insertion cost/ unit	$535		$405	
Maintenance cost/ unit	$109		$195	
Fail to withdraw/ unit	$303		$480	
Total per patient	$35,035/37 pts	$947	$38,867/36 pts	$1,080
Net savings per unit		$133		

N/A = not applicable; pts = patients.

blood return resulted in an additional $480 of cost per unit to the nonvalved port group, compared to an additional $303 cost per unit to the valved port group. In total, the lower costs associated with port maintenance and failure to achieve blood return associated with the PASV port offset the higher acquisition cost and resulted in a net savings of $132 per unit in the valved port group compared to the nonvalved group.

Comments

Venous access devices are valuable instruments for patients who require intravenous medications, chemotherapy, hydration, and nutrition [8]. Earlier long-term venous access devices were described by Broviac et al and then by Hickman et al [9,10]. These devices had the disadvantage of containing a subcutaneous cuff. Totally implantable access ports have the advantages of not requiring an external dressing, allowing more patient activity, requiring only monthly maintenance flushing, and are associated with fewer infectious complications compared to tunneled catheters [11,12]. While totally implantable venous access devices represent a significant improvement from previous models, these devices still have a reported complication rate of 11% to 25% [2,5,11]. One of the more commonly reported problems with totally implantable ports is catheter tip thrombosis [8]. Thrombosis and catheter occlusion is usually initially seen as an inability to withdraw blood with needle access. Ameliorating this difficulty may simply require catheter manipulation and flushing, or may result in additional studies and procedures. Furthermore, catheter tip thrombosis can result in patient hospitalization, emergency room visits, interruption of therapy, and device replacement. This can have a substantial impact on the health care system, including increased office costs, staff time, and additional diagnostic evaluation [12].

A previous study randomized 365 patients to PICCs with PASV valves and standard nonvalved PICC lines. Overall complications including catheter occlusion and infection occurred in 6.6% of subjects in the valved group and in 14.2% of subjects in the nonvalved group ($P = 0.02$). Catheter occlusion by itself occurred in 3.3% versus 7.1% in the valved and nonvalved groups, respectively, but this did not reach statistical significance [7].

Our study demonstrated that the PASV port had significantly less instances of difficulty drawing blood during access. This resulted in less infusion room and nurse-access time, as well as fewer instances where chest radiography, physician consultations, and t-PA infusions were required. Our cost analysis demonstrated that while the material unit cost of the PASV port is higher than the BardPort, the increased maintenance costs associated with the BardPorts actually resulted in a net savings of $132 per unit with the PASV ports. Furthermore, true cost savings may be difficult to quantify. Delays in chemotherapy treatment may result in

premixed solutions not being used, additional office visits, and delays in patient treatment, all of which carry costs that cannot easily be quantified.

The exterior designs of the ports are similar; therefore, as expected, there was no statistical difference in infectious or mechanical complications between valved port group and the nonvalved port group. There were 2 episodes of postoperative port-site cellulitis, both of which occurred in the valved port group. Both episodes occurred before first access and use of the port and are considered perioperative complications not due to catheter use or design. A single patient in each group was hospitalized for catheter-related sepsis. Each patient required intravenous antibiotics and port removal. These occurrences are both less than the reported rate of 5% in the literature for the number of patients with subcutaneous ports treated for sepsis [11,13]. Other major complications such as venous thrombosis and catheter fracture are much less common, occurring at rates of 2.0% to 2.5% and 0.2%, respectively [13–15]. The present study was not powered to detect significant differences in the aforementioned complications due to their low incidence, and would not be expected due to the similar port design.

Because each port type has different maintenance infusions (BardPort using heparinized saline vs. PASV port using normal saline), this study was not completely blinded to the nursing staff. The infusion room nurses were aware of the port type in use; however, they were not aware of study goals or initial outcomes. Additionally, our institution has several infusion room centers, each employing different infusion nurses, which removes a possible single-observer bias to the study.

This current study reports on the first clinical trial demonstrating an advantage to using a totally implantable central venous port that employs a PASV valve system. Theoretically, a proximal valve in the port system prevents blood reflux during infusion needle removal and during episodes of increased intrathoracic pressures seen with coughing or valsalva. This feature may be responsible for the observed reduction in blood return difficulties seen in the studied PASV port. The fewer incidences of blood withdraw problems equated to less infusion room time, less nursing accession time, and fewer uses of t-PA. Because of these benefits, the PASV port has become the port of choice at this institution.

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Discussion

Jeffery Saffle, M.D. (Salt Lake City, UT): In the current era of evidence-based medicine, many of us have become increasingly skeptical about the competing claims from manufacturers of various medical devices, especially in the absence of data. I therefore congratulate Dr Carlo and his colleagues on designing and performing a simple, straightforward, randomized controlled, single-institution trial, aimed at answering a very straightforward question. Is there a difference between valved and nonvalved implantable ports? I think that many of us, instead of spending endless hours arguing the merits of various products or sharing our anecdotes, would do well to follow this example. It's previously been observed that "the plural of anecdote is not data." Here is an example of a group who spent the time and trouble to generate data, thereby obviating the repetitive and pointless citation of anecdotes in the future. They demonstrated that valve-containing implantable port catheters had a lower incidence of thrombosis and more trouble-free use. Their data were also very illuminating, at least to me, in highlighting many of the hidden costs associated with even the most minor of problems arising from the use of these devices, including a cost of at least $500 to declot an occluded catheter. Also, over 13 hours of additional nursing

work were needed to care for the nonvalved catheters. Some of these other costs were equally eye opening. All of that represents the good news of this study. There are some weaknesses that lead me to my questions. First, the study contained the magic words "randomized" and "controlled," but I did not see that it was blinded. Obviously the surgeons cannot be blinded to catheter placement, but, since the ports are entirely hidden beneath the skin, couldn't the protocols have been amended so that the nurses did not know which port was in place? Some of the data collected relied on nurses' subjective assessments. Wouldn't this have improved the quality of your data and perhaps its believability? Secondly, I did not see any record of ports having to be replaced because of thrombosis in either group. Did this occur and was there a difference between groups? My final comment is a bit more speculative and, and perhaps provides a bit of guidance for those of us who would like to emulate your example and design simple trials within our own institutions. It was not mentioned that this study was supported financially by the company whose product was found to be superior. Well, that may not have influenced the study design or the results, but it will perhaps inevitably color the reception and credibility given this paper. I'd be interested in knowing exactly how this support was provided. Importantly, my institutional review board will not allow me to design a randomized trial in which half of the patients are charged more than the other half of the patients. So I would like to know how that financial difference was worked out for this study.

Answer

John Carlo, M.D. (Dallas, TX): To answer your first question, although both ports appear identical on the surface, the study was not blinded to the nursing staff, in a sense, because each port used a different flush solution, either heparinized saline or normal saline. Although a completely blinded study would have been optimal, that design was too logistically difficult and would have been more costly to perform. We do not feel that the nurses were biased in any way toward one or the other port in this study.

The second question was regarding venous thrombosis. One patient in each group had a symptomatic venous thrombosis. These were both in patients nearing the end of their treatment for breast cancer. Both patients were successfully treated with anticoagulation and port removal following completion of their treatment.

This study was supported by a research grant from Boston Scientific to help pay for our administrative costs. The costs of the port were covered by patient's insurance. Although there is a difference in the cost between the devices themselves, they are both Food and Drug Administration–approved devices and were used interchangeably based on surgeon preference prior to this study. Thus, patients were not required to pay any difference in the device costs. We do feel that the difference in cost is important, in that it seems to be offset by improved performance of the valved port.

Question

Mark Jensen, M.D. (Fargo, ND): My first question is with the placement of the catheters. You mentioned that some were placed in the subclavian position and some in the internal jugular vein position. How many were in the internal jugular vein and how many in the subclavian? My second question relates to the subclavian position. When you send your patient down for your postoperative chest x-ray, the technician will put the arms up. What you need to do is, particularly with the subclavian catheters, is have the arms down to look for the pinch off sign. Were you able to do that specifically in your study and did that pinch off sign lead to problems?

Answer

John Carlo, M.D. (Dallas, TX): Catheter placement was roughly equally distributed between the internal jugular and subclavian routes based on surgeon preference. In the subclavian position we are careful to evaluate for a "pinch" of the catheter as it travels under the clavicle both with intraoperative fluoroscopy and with the postoperative chest radiograph. This is usually due to a catheter that traverses the periostium of the clavicle or is trapped between the clavicle and the first rib. We would consider a catheter with a "pinch" to be improperly placed and none of our the catheters in this study were found to be partially obstructed at the clavicle. Postoperative chest films are taken in the upright position with the arms at the sides.