American Journal of Infection Control 48 (2020) 281–284

Contents lists available at ScienceDirect

American Journal of Infection Control

journal homepage: www.ajicjournal.org

Major Article

Impact of needle-free connectors compared with 3-way stopcocks on catheter-related bloodstream infection rates: A meta-analysis

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Key Words:
Mechanical valve
Needleless connector
Split septum
Negative-, positive-, and neutral-displacement needleless connectors
Open system connectors

Background: Needle-free connectors (NFCs) were introduced to eliminate the use of needles in intravascular catheters, and their newest generations were designed to improve patient safety and reduce catheter-related bloodstream infection (CRBSI) risks. The aim of this meta-analysis was to compare NFCs with 3-way stopcocks (3WSCs) and their effects on CRBSI rates.

Methods: A meta-analysis was conducted using a research protocol consistent with the PRISMA statement for reporting meta-analyses. The Cochrane Database of Systematic Reviews and MEDLINE were searched for relevant randomized studies published from January 2000 to September 2018.

Results: We identified and selected for the meta-analysis 8 studies comparing CRBSI rates (according to the Centers for Disease Control and Prevention's National Healthcare Safety Network definition) associated with NFCs utilizing negative-displacement, neutral-displacement, or positive-displacement devices with rates for 3WSCs. Relative risk was 0.53 with a 95% CI of 0.28 to 1.00, and the relative difference was −0.018 with a 95% CI of −0.039 to 0.004.

Conclusions: CRBSI risk was statistically higher for 3WSCs compared to NFCs.

BACKGROUND

In addition to being among the most prevalent occupational accidents, needlestick injuries are also among the most preventable ones. Health care workers (HCWs), particularly nurses and physicians but also cleaning staff and others, are at high risk for sustaining a percutaneous injury. These injuries not only expose HCWs to more than 20 different bloodborne pathogens (BBPs) that can be acquired from a patient but also expose patients to the transmission of diseases from HCWs. It is estimated that 384,000 percutaneous injuries occur in US hospital settings per year, with 61% (236,000) of them being hollow-bore needlestick injuries and 23% of them occurring during surgical procedures.[1] HIV as well as hepatitis B and C viruses and other BBPs constitute infectious hazards in health care settings. Their transmission has been reported to be primarily from patient to HCW and from patient to patient, in addition to, although rarely, from HCW to patient. The risk of BBP transmission is largely preventable; however, accidental punctures with contaminated instruments must be entirely avoided to lower this risk.[2]

The first US standard to address occupational exposure to bloodborne pathogens and needlestick and sharps injuries among HCWs was issued in1991 by the Occupational Safety and Health Administration.[3] This standard was revised through enactment of the Needlestick Safety and Prevention Act in 2001, after which needle-free connectors (NFCs), also referred to as closed systems (CSs), were introduced into clinical practice with the purpose of excluding the use of needles on intravascular catheters.[3] Before the introduction of NFCs, 3-way stopcocks (3WSCs), also referred to as open systems (OSs), were used.

To prevent accidental needlestick injuries and BBP infections and to comply with Occupational Safety and Health Administration regulations and the Needlestick Safety and Prevention Act, various designs for safety devices have been developed. Nevertheless, considerable increases in catheter-related bloodstream infection (CRBSI) rates have been reported since NFCs came onto the market.[4] As a result, infection control practices involving these devices were brought into focus, leading to lower infection risks. Negative-displacement mechanical NFCs were introduced to reduce the risk of needle use with these devices. Also, to decrease intravenous (IV) line occlusions and CRBSI risks, positive-displacement NFCs were introduced,

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Conflicts of interest: None to report.

https://doi.org/10.1016/j.ajic.2019.08.015
0196-6553/

resulting in fewer CRBSI outbreaks being associated with these NFCs.[4,5] Eventually, the Food and Drug Administration required US manufacturers of positive-displacement NFCs to provide evidence showing that their devices were associated with lower or equal risks of CRBSI in comparison with negative-displacement NFCs.

To date, newly designed features of NFCs include a solid, flat, smooth access surface for effective disinfection; a visible fluid path to enable clinicians to assess the efficacy of their flush technique; 1-part activation of the fluid path for effective flush; and an open fluid pathway to provide a high flow rate and avoid hemolysis, among other desired safety features (eg, tight septum seal, minimal internal complexity, ability to flush with saline alone).[6] The objective of this meta-analysis was to compare CRBSI risks between patients using OSs and CSs.

Needle-free connectors

NFCs provide needle-free access at the hub end of the catheter for IV medication administration, fluid infusion, or withdrawal of blood samples or to connect administration sets to the intravascular catheters. Needle-free connectors include split-septum connectors and luer-activated mechanical valves. The standard split-septum connectors or negative-reflux caps do not have internal mechanisms and are pre-pierced to allow access by a blunt cannula to open the fluid pathway for IV fluid infusion or medication administration.

Based on their internal membrane function, mechanical valves are classified as negative-, neutral-, or positive-displacement types. Mechanical valves have an internal membrane or valve and require a mating luer connector when flushing or administering IV fluids or medications. The syringe tip or the tip of the IV tubing is directly inserted into the cap without the need for a blunt needle.[7] The design of positive-pressure valves is aimed at preventing retrograde blood flow inside the catheter after the luer is disconnected to prevent thrombotic occlusions and also to avoid catheter hub and endoluminal microbial contamination, assuming that aseptic techniques are followed.[8]

Types of IV needle-free connectors

- *Negative-displacement NFCs* allow blood reflux into a vascular access device lumen upon disconnection due to movement of valve mechanism or removal of the syringe or set. With negative-displacement mechanical valves, the luer caps must be clamped prior to removing the syringe or tubing set to prevent blood from backing up into the catheter.
- *Positive-displacement NFCs* allow a small amount of fluid to be held in the device; upon set or syringe disconnection, this fluid is pushed through the catheter lumen to clear any blood that refluxed into the lumen. The positive-displacement valves, also called positive-pressure valves, have a fluid reservoir that creates a positive-displacement movement or pressure and should not be clamped when disconnecting the syringe or IV administration sets.
- *Neutral-displacement NFCs* contain an internal mechanism designed to prevent blood reflux into the catheter lumen upon connection or disconnection. For neutral-displacement valves, there is no displacement of fluid into the catheter when connecting or disconnecting the syringe or tubing, and their use requires no change in clamping practices.
- *3-way stopcocks* consist of a valve or turning plug that controls the flow of fluid from a container through a tube. A 3WSC can be used on IV tubing to turn off one solution and turn on another. It is open to the air, without a membrane, when the cover is not in place and for that reason is considered to be an open IV system.

METHODS

Data sources

We developed a research protocol and data collection tools consistent with PRISMA recommendations.[9] We searched the MEDLINE database for relevant studies published from January 2000 to September 2018, as well as ClinicalTrials.gov, Embase, and the Cochrane Database of Systematic Reviews.

Study selection and data extraction

Study inclusion criteria were randomized controlled trials or observational studies that reported CRBSI rates in patients with positive-, negative-, or neutral-displacement devices compared to 3WSC connectors. For the search, we used the following medical subject headings and key words: catheter-related bloodstream infection, bloodstream infections, central venous catheter-associated infections, mechanical valve, needle-free connector, needle free connector, needle less connector, needless connector, split septum, negative-displacement needle less connector, positive-displacement needle less connector, neutral-displacement needle less connector, open system connectors, three ways stop cock.

An Internet search was conducted independently by 2 investigators. All abstracts identified were read independently by 2 investigators (1 with a PhD, 1 with an MD). Disagreement was resolved by discussions with a third investigator. Data extracted from these studies on standardized forms included study design; setting; patient population; facility location; and number of CRBSIs (numerator) and number of central line (CL) days (denominator) during the study for needle-free device periods compared to 3WSC device periods. We recorded CRBSI incidence density (infections per 1000 CL days) at each site.

Meta-analysis

An overall estimate of relative risk (RR) was calculated treating the study as a random effect. A closed system was defined as the treatment (ie, probability in the numerator); consequently, a RR of 1 indicates similar risk, and a RR of <1 indicates that the closed system has less risk then the open system. The overall RR estimate is complicated by the 0 open system positives reported by Khalidi in 2009.[10] A 0 in a numerator or denominator of a fraction is mathematically intractable. Generally, 0 events are handled by

- Dropping any 0 event studies from the overall estimate
- Adding a small number, such as 1/2, to the 0 event or to all of the events

Neither approach is completely satisfying. Dropping a study or studies introduces a potential bias to the overall estimate,[11] and the outcome of adding a small number is sensitive to the number chosen and method used (ie, different conclusions can be reached depending on the number or method used). For the analysis reported here, the 0-event study was excluded from the estimate of overall RR. To mitigate any bias introduced by this exclusion, the RR analysis was supplemented with an estimate of the overall relative difference (RD), as suggested by Keus et al.[12] The overall RD estimate is robust to 0 events.

RESULTS

We selected 8 randomized, prospective in vivo studies that compared CRBSI rates associated with the use of OSs versus CSs. Table 1 summarizes the counts and rates for the 8 articles selected for the meta-analysis, and Table 2 shows the RR and RD estimates and 95% CIs for the individual studies and overall. The RR null value is 1; the RD null value is 0. The CI for the overall RR estimate is strictly lower than 1, implying that the risk is lower with the CSs. However, the CI for the overall RD estimate includes 0, implying that a conclusion of "no difference" cannot be ruled out. Details are given in Table 2 and depicted in Figure 1.

DISCUSSION

In this meta-analysis, we identified 8 relevant randomized studies published from January 2000 to December 2018 in which CRBSI rates for NFCs with negative-displacement devices, neutral-displacement devices, or positive-displacement devices were compared with cases with 3WSCs. In a pre-post study conducted by Royer et al,[20] a swabable positive-displacement device (MaxPlus clear needleless connector; Becton Dickinson, Franklin Lakes, NJ) was compared to another non-swabable positive-displacement device (MaxPlus). For the swabable positive-displacement device, the CRBSI rate was 0.84 per 1000 CL days; for the non-swabable positive-displacement device, the CRBSI rate was 1.73 per 1000 CL days.

In a pre-post study conducted by Wheeler et al,[21] a negative-displacement device was compared with another negative-displacement device. The authors observed an unexpected increase in the rate of CRBSI at their institution during August 2009. They discovered that the Spiros closed male connector (ICU Medical; San Clemente, CA) had been introduced in these 2 units around the same time that the cluster of infections occurred. Based on this information, use of this device was discontinued, and the CRBSI rate and distribution of causative microorganisms returned to their previous baseline values.

In a meta-analysis conducted by Tabak et al,[22] positive-displacement devices were compared with negative- or neutral-displacement devices. Studies reporting the CRBSIs in patients using the positive-displacement NFC (study NFC) compared with negative- or neutral-displacement NFCs were analyzed. In the comparator period, total CL days were 111,255, and the CRBSI rate was 1.5 events per 1000 CL days. In the study NFC period, total CL days were 95,383, and the CRBSI rate was 0.5 events per 1000 CL days. The pooled CRBSI RR associated with the study NFC was 0.37 (95% CI, 0.16-0.90). The NFC with an improved engineering design was associated with lower CRBSI risk.

In a pre-post study conducted by Wallace et al,[23] the use of a non-swabable positive-displacement NFC (MaxPlus) resulted in a CRBSI rate of 2.9/1000 in 2010. After implementation of the swabable positive-displacement NFC, the CRBSI rate dropped and remained statistically stable: 0.8 per 1000 CL days (95% CI, 0.1-3.0) in 2011, 0 (95% CI, 0.0-1.8) in 2012, and 0.91 (95% CI, 0.1-3.3) in 2013.

In a pre-post study conducted by Casey et al,[24] a positive-displacement device was compared with a neutral-displacement device. There were 557 needle-free IV access devices connected to 167 catheters (86 in the neutral- and 81 in the positive-displacement group) from 157 patients that were studied (2 catheters were studied in 10 patients). There was no difference in the rates of CRBSI among the first neutral- and positive-displacement device periods and the second neutral-displacement device period (7.52, 6.62, and 6.30 per 1000 patient days, respectively) (first neutral-displacement device vs positive-displacement device, $P = .60$; first neutral-displacement device vs second neutral-displacement device, $P = .56$; positive-displacement device vs second neutral-displacement device, $P = .85$). There was also no difference in the rates of non-mucosal barrier injury, laboratory-confirmed CRBSIs among the 3 periods (4.30, 3.42, and 2.00 per

Table 2
Relative risk and relative difference estimates for the individual studies and overall

Source	Relative risk (95% CI)	Relative difference (95% CI)
Casey et al (2003)[13]	0.37 (0.22, 0.61)	−0.114 (−0.166, −0.062)
Yebenes et al (2004)[14]	0.15 (0.02, 1.20)	−0.004 (−0.008, 0.000)
Esteve et al (2007)[15]	1.12 (0.74, 1.69)	0.000 (−0.001, 0.002)
Casey et al (2007)[16]	0.05 (0.01, 0.38)	−0.095 (−0.138, −0.052)
Yebenes et al (2008)[17]	0.14 (0.02, 1.08)	−0.029 (−0.053, −0.004)
Khalidi et al (2009)[10]	NA	0.002 (−0.002, 0.006)
Gonzalez Lopez et al (2013)[18]	0.86 (0.41, 1.83)	−0.001 (−0.006, 0.004)
Rosenthal et al (2015)[19]	0.35 (0.16, 0.76)	−0.004 (−0.007, −0.001)
Overall	0.40 (0.20, 0.80)	−0.025 (−0.052, 0.003)

NA, not available.

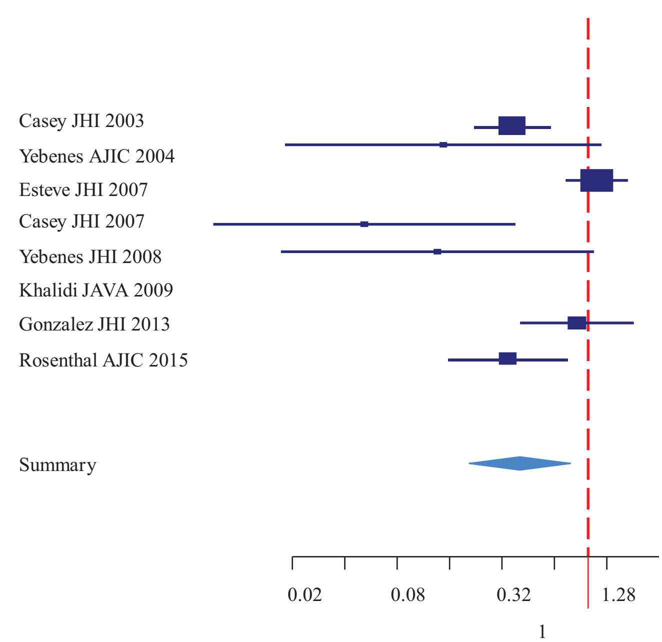

Fig 1. Relative risks.

Table 1
Summary of article metrics

Source	Open system			Closed system		
	Catheter days	Positives	Rate*	Catheter days	Positives	Rate*
Casey et al (2003)[13]	306	55	179.7	274	18	65.7
Yebenes et al (2004)[14]	1,404	7	5.0	1,362	1	0.7
Esteve et al (2007)[15]	10,462	43	4.1	10,195	47	4.6
Casey et al (2007)[16]	200	20	100.0	193	1	5.2
Yebenes et al (2008)[17]	241	8	33.2	221	1	4.5
Khalidi et al (2009)[10]	768	0	0.0	864	2	2.3
Gonzalez Lopez et al (2013)[18]	2,096	14	6.7	2,257	13	5.8
Rosenthal et al (2015)[19]	4,061	26	6.4	3,619	8	2.2

*Rates are per 1000 catheter days.

1000 patient days, respectively) (first neutral-displacement device vs positive-displacement device, $P = .49$; first neutral-displacement device vs second neutral-displacement device, $P = .11$; positive-displacement device vs second neutral-displacement device, $P = .19$). Fewer septa and internal fluid pathways were contaminated in the positive-displacement device group compared to the neutral-displacement device group. Most microorganisms isolated were skin or environmental bacteria.

Limitations

This meta-analysis had several limitations. Bias may have been introduced in the selection and location of studies, resulting in publication bias, English language bias, and citation bias. Also, studies from limited-resource countries are more likely to be published in journals indexed in a literature database, thus introducing database bias. Finally, this meta-analysis did not include sensitivity or subgroup analyses or meta-regression to examine the possible introduction of biases in the study selection process.[25]

CONCLUSIONS

The results of this meta-analysis showed that CRBSI risk was statistically higher for 3WSCs compared to NFCs.

Acknowledgments

I would like to thank Karen J. Byron, Becton Dickinson, Corporate Statistics Manager, who collaborated with this meta-analysis, and Debora Lopez Burgardt, who assisted in its drafting.

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