

# Sonication for Diagnosis of Catheter-Related Infection Is Not Better Than Traditional Roll-Plate Culture: A Prospective Cohort Study With 975 Central Venous Catheters

Stefan Erb,<sup>1</sup> Reno Frei,<sup>2</sup> Katharina Schregerberger,<sup>1</sup> Marc Dangel,<sup>1</sup> Danica Nogarth,<sup>1</sup> and Andreas F. Widmer<sup>1</sup>

Divisions of <sup>1</sup>Infectious Diseases and Hospital Epidemiology and <sup>2</sup>Clinical Microbiology, University Hospital Basel, Switzerland

**This prospective randomized controlled study with 975 nontunneled central venous catheters (CVCs) showed that the semiquantitative roll-plate culture technique (SQC) was as accurate as the sonication method for diagnosis of catheter-related infections. Sonication is difficult to standardize, whereas SQC is simpler, faster, and as reliable as the sonication method for culturing CVCs.**

**Keywords.** semiquantitative roll-plate method; sonication; central venous catheter; catheter-related bloodstream infections.

The diagnosis of catheter-related infection requires a positive result by the semiquantitative roll-plate culture method (SQC) described by Maki et al [1] or the quantitative sonication technique [2, 3] of the central venous catheter (CVC) and a matching strain from percutaneously drawn blood cultures in cases of catheter-related bloodstream infection (CR-BSI). Both techniques are recommended in the current Centers for Disease Control and Prevention and Infectious Diseases Society of America guidelines for diagnosis and management of catheter-related infections as equivalent methods [4, 5]. Sonication is considered to have a higher sensitivity than SQC by detecting intraluminal and extraluminal bacteria, whereas SQC only detects extraluminal bacteria [6–8]. However, more recent studies were unable to confirm the advantage of the sonication method,

even in tunneled long-term catheters where endoluminal contamination is thought to be the most frequent route of microbial colonization [9–11]. Furthermore, sonication is time-consuming, difficult to standardize, and complicated to perform.

In a prospective, observational, randomized controlled trial from 2005 until 2009 at the University Hospital of Basel, Switzerland, we compared the SQC with the quantitative sonication method for diagnosis of significant catheter colonization.

## MATERIALS AND METHODS

All consecutive nontunneled CVCs with a minimal length of 10 cm were included in our study. CVCs were cut into 2 equal 5-cm-sized segments, in a subcutaneous part and a catheter tip, and randomly processed with the SQC by Maki et al [1] and an improved quantitative sonication method published elsewhere [12]. Randomization occurred in the microbiology laboratory: On even days, the catheter tip was processed by the roll plate and the subcutaneous segment of the catheter was processed with the sonication method, and vice versa on odd days.

Catheter colonization was defined as  $\geq 15$  colony-forming units (CFU) per 5-cm-sized catheter segment for the SQC and/or  $\geq 100$  CFU per 5-cm-sized catheter segment for sonication [1, 4, 6]. Our data were also recalculated using different cut-offs of  $\geq 5$  CFU for SQC and  $\geq 1000$  CFU for sonication.

Diagnosis of CR-BSI was based on current guidelines [4, 13] and required a catheter tip colonization as described above, with the same phenotypic microorganism isolated from blood culture or a differential time to positivity of  $\geq 2$  hours for the peripheral vs the CVC blood culture. For CR-BSI with skin contaminants such as coagulase-negative staphylococci, systemic inflammatory response syndrome (SIRS) with at least 2 SIRS criteria had to be present [14].

We calculated a sample size of  $>800$  CVCs to detect an absolute 5% difference with 90% power. Paired proportions from catheters were compared using the McNemar test with 95% confidence intervals (CIs). Continuous variables from independent patient data were analyzed by Student *t* test. A *P* value of  $<.05$  was considered to be statistically significant. Data were analyzed using the SPSS software package, version 21.0.

## RESULTS

A total of 975 nontunneled CVCs from 800 patients were examined with both the SQC and the new sonication method. The

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Correspondence: Andreas F. Widmer, MD, MS, Division of Infectious Diseases and Hospital Epidemiology, University Hospital Basel, Petersgraben 4, 4031 Basel, Switzerland (andreas.widmer@usb.ch).

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**Table 1. Detection Rate of Catheter Colonization in All 975 Examined Catheters by Use of Different Cutoffs Between Semiquantitative Culture and Sonication**

SQC $\geq 15$ CFU and/or Sonication $\geq 100$ CFU (n = 217)				SQC $\geq 5$ CFU and/or Sonication $\geq 100$ CFU (n = 235)			
	SQC+	SQC-		SQC+	SQC-		
Sonication+	157	27	184	Sonication+	165	19	184
Sonication-	33	758	791	Sonication-	51	740	791
	190	785	975		216	759	975
OR, 0.82 (95% CI, .49–1.36); $P = .52$				OR, 0.37 (95% CI, .22–.63); $P < .001$			
SQC $\geq 5$ CFU and/or Sonication $\geq 1000$ CFU (n = 224)				SQC $\geq 15$ CFU and/or Sonication $\geq 1000$ CFU (n = 203)			
	SQC+	SQC-		SQC+	SQC-		
Sonication+	122	8	130	Sonication+	118	12	130
Sonication-	94	751	845	Sonication-	73	772	845
	216	759	975		191	784	975
OR, 0.085 (95% CI, .04–.18); $P < .001$				OR, 0.16 (95% CI, .09–.30); $P < .001$			

Abbreviations: CFU, colony-forming units; CI, confidence interval; OR, odds ratio; SQC, semiquantitative culture.

SQC was performed in 481 (49.3%) catheter tips and 494 (50.7%) subcutaneous segments, and vice versa with the sonication method.

Significant colonization was detected in 217 of the 975 (22.3%) catheters with at least 1 of the 2 methods by use of currently recommended cutoff of  $\geq 15$  CFU for SQC and  $\geq 100$  CFU for sonication. Fifty-two (24%) patients had a CR-BSI that fulfilled study criteria. The remaining 165 catheters were derived from patients with secondary bloodstream infections not related to the catheter or asymptomatic patients without signs of infection (for baseline characteristics, see the [Supplementary Table](#)).

When using the established cutoff of  $\geq 15$  CFU for SQC and  $\geq 100$  CFU for the sonication method, the SQC method detected colonization in 190 (87.6%) and sonication detected colonization in 184 (84.8%) of the 217 catheters (Table 1). Discrepant results occurred in 27 (SQC positive, sonication negative) and in 33 (SQC negative, sonication positive) processed catheters. Thus, no significant difference of likelihood of detection between the 2 methods could be found (odds ratio [OR], 0.82 [95% CI, .49–1.36];  $P = .52$ ).

When using a lower cutoff of  $\geq 5$  CFU for the SQC method, the detection rate of SQC increased to 91.9%, which was

**Table 2. Detection Rate of Catheter Colonization by Semiquantitative Culture and Sonication<sup>a</sup>**

CVCs With a Dwelling Time $>7$ d (n = 165)				CVCs With a Dwelling Time $\leq 7$ d (n = 52)			
	SQC+	SQC-		SQC+	SQC-		
Sonication+	119	19	138	Sonication+	38	8	46
Sonication-	27	0	27	Sonication-	6	0	6
	146	19	165		44	8	52
OR, 0.70 (95% CI, .39–1.27); $P = .30$				OR, 1.33 (95% CI, .46–3.84); $P = .79$			
CVCs From Patients With CR-BSI (n = 52)							
	SQC+	SQC-					
Sonication+	37	7	44				
Sonication-	8	0	8				
	45	7	52				
OR, 0.875 (95% CI, .32–2.41); $P = 1.00$							

Abbreviations: CI, confidence interval; CR-BSI, catheter-related bloodstream infection; CVCs, central venous catheters; OR, odds ratio; SQC, semiquantitative culture.

<sup>a</sup> SQC cutoff of  $\geq 15$  colony-forming units (CFU) and sonication cutoff  $\geq 100$  CFU in the subgroup of patients with CVC dwelling time  $>7$  and  $\leq 7$  days and patients with CR-BSI.

**Table 3. Frequency of Isolated Pathogens in All 217 Colonized Catheters<sup>a</sup>**

Microorganisms	Total (n = 217) <sup>b</sup>	SQC+/SONIC+ (n = 157)	SQC+/SONIC- (n = 33)	SQC-/SONIC+ (n = 27)	P Value
CoNS	148 (68.2%)	106	28	14	.045*
<i>Staphylococcus aureus</i> <sup>c</sup>	13 (6.0%)	12	1	0	
<i>Enterococcus</i> spp	7 (3.2%)	5	1	1	
Gram-positive bacteria <sup>d</sup>	4 (1.8%)	1	2	1	
Gram-negative bacteria	36 (16.6%)	26	1	9	.021**
Enterobacteriaceae	26	18	1	7	
<i>Pseudomonas aeruginosa</i>	6	5	0	1	
<i>Stenotrophomonas maltophilia</i>	2	2	0	0	
Others <sup>e</sup>	2	1	0	1	
<i>Candida</i> spp	9 (4.1%)	7	0	2	

SQC+:  $\geq 15$  colony-forming units (CFU); SQC-:  $< 15$  CFU; SONIC+:  $\geq 100$  CFU; SONIC-:  $< 100$  CFU.

Abbreviations: CoNS, coagulase-negative staphylococci; SONIC, sonication; SQC, semiquantitative culture.

<sup>a</sup>With cutoffs of  $\geq 15$  CFU for SQC and  $\geq 100$  CFU for SONIC.

<sup>b</sup>Main pathogen detected by at least 1 of the 2 methods of all 217 colonized catheters with cutoff of  $\geq 15$  CFU for SQC and  $\geq 100$  CFU for SONIC. Thirty-three catheters had polymicrobial colonization with an additional 40 microorganisms detected with at least 1 of the 2 methods, but in a lesser amount than the main pathogen: 26 CoNS, 7 *Corynebacterium* spp, 3 *Streptococcus* spp, 2 *Enterococcus* spp, 1 *Stenotrophomonas maltophilia*, and 1 yeast (not included in the table).

<sup>c</sup>One *S. aureus* was methicillin-resistant.

<sup>d</sup>Gram-positive bacteria: *Streptococcus* spp, *Corynebacteria* spp.

<sup>e</sup>Gram-negative bacteria, others: *Acinetobacter baumannii*, *Hafnia alvia*.

\*Odds ratio (OR), 0.5 (95% confidence interval [CI], .26–.95).

\*\*OR, 9.0 (95% CI, 1.14–71.04).

significantly better compared with sonication with a cutoff of  $\geq 100$  CFU and  $\geq 1000$  CFU (both  $P < .001$ ). By raising the sonication cutoff to  $\geq 1000$  CFU (with cutoff  $\geq 15$  CFU for SQC), the performance of this method became worse compared with SQC ( $P < .001$ ; Table 1).

From the 217 CVCs with significant colonization using a cutoff of  $\geq 15$  CFU for SQC and/or  $\geq 100$  CFU for sonication, 52 (24.0%) were in place for a short time ( $\leq 7$  days), and 165 (76.0%) were in place for  $> 7$  days (Table 2). In both of these groups, SQC showed noninferiority to sonication ( $P = .79$  and  $P = .30$ , respectively).

In the 52 patients with CR-BSI, 45 (86.5%) and 44 (84.6%) CVCs were found to be colonized by the SQC and the sonication technique, respectively; thus, the likelihood of detection did not differ between the 2 methods ( $P = 1.00$ ; Table 2).

The likelihood of detection of colonization between SQC and the sonication method was similar in subclavicular (OR, 1.50 [95% CI, .534–4.24];  $P = .607$ ) and jugular (OR, 0.69 [95% CI, .38–1.263];  $P = .291$ ) CVCs, and also when examining the catheter tips (OR, 1.0 [95% CI, .46–2.18];  $P = .85$ ) and the subcutaneous segments (OR, 0.70 [95% CI, .35–1.39];  $P = .35$ ) (data not shown).

The distribution of the 217 isolated main pathogens showed a predominance of coagulase-negative staphylococci, followed by gram-negative bacteria and *Staphylococcus aureus* (Table 3). When comparing the 2 methods, coagulase-negative staphylococci were more frequently detected by SQC (OR, 0.5 [95% CI, .26–.95];

$P = .045$ ), whereas gram-negative bacteria were better detected with the sonication method (OR, 9.0 [95% CI, 1.14–71.04];  $P = .021$ ).

## DISCUSSION

In this randomized controlled study of 975 nontunneled CVCs, we demonstrated that the use of an improved quantitative sonication technique [12] to detect catheter colonization is not superior to the SQC method by Maki et al when using a recommended cutoff of  $\geq 15$  CFU for SQC and  $\geq 100$  CFU for sonication—neither in patients with a CR-BSI nor in catheters with a long dwelling time of  $> 7$  days. The noninferiority of the SQC method as shown in our results is in accordance with the findings of other recent studies [9–11]. Furthermore, the quantitative sonication method requires special equipment, is difficult to standardize, and is time-consuming and complicated to perform, making it less attractive for routine microbiological catheter diagnostics.

The strength of our study is the large sample size of almost 1000 CVCs that we could examine simultaneously with both methods at the same time on a 5-cm-sized catheter tip and adjacent subcutaneous segment. Hence, direct comparison of the 2 methods is very reliable, whereas serial processing of catheters by different detection methods as described in a former study suffers from possible loss of microbial colonies during serial examination [11]. As the yield of detection of colonization of catheter tips and subcutaneous segments was similar as shown in

previous studies and in our own data [6], the comparison of catheter tip and subcutaneous segment cultures is most likely appropriate.

When analyzing our results with different cutoffs for both methods, the SQC was always equal or better than sonication in the detection of catheter colonization. However, the additional benefit of a lower SQC cutoff of  $\geq 5$  CFU/catheter segment remains debatable due to loss of specificity, but could be useful in antibiotic-pretreated patients.

The distribution of the 217 pathogens in our study was as expected. In case of polymicrobial catheter colonization, we only analyzed the main pathogen with the highest CFU count. As only 33 catheters showed polymicrobial colonization, we considered this approach to be feasible. Whereas coagulase-negative staphylococci were detected significantly better by SQC, gram-negative bacteria were better detected with the sonication method. This is particularly interesting because gram-negative bacteria are usually more susceptible than gram-positive bacteria to the effect of ultrasound and thus more difficult to detect [15]. Explanations remain hypothetical and may imply a more gentle sonication technique, a weaker adhesion to the surface due to less biofilm formation, or a potentially mainly endoluminal origin of gram-negative bacteria. However, in the subset of the 52 patients with CR-BSI, no difference was seen between the 2 methods.

Our study has some limitations. We did not distinguish between antimicrobial-coated and -uncoated CVCs in our study, which could have influenced the results; however, only 8% of the analyzed CVCs were submitted from the transplant unit, where coated catheters are routinely inserted. In addition, only first-generation chlorhexidine/silver sulfadiazine-coated CVCs are used that are coated only at the outer surface of the catheter. But this would have rather lowered the sensitivity of the SQC method.

Furthermore, we did not collect data about administered systemic antibiotics over the CVC that could have influenced the colonization rate. It is well known that antimicrobial treatment can lower the diagnostic yield of catheter tip culture. As the antibiotics are usually administered through the catheter, endoluminal microbes might be compromised more than extraluminal bacteria, which could impair the sensitivity of the sonication more than the roll-plate method [10].

In conclusion, this prospective randomized controlled study with 975 nontunneled CVCs showed that the SQC was as accurate as the sonication method for diagnosis of catheter-related infections. Sonication is difficult to standardize, whereas SQC is simpler, faster, and as reliable as the sonication for culturing CVCs.

## Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online (<http://cid.oxfordjournals.org>). Supplementary materials consist of data

provided by the author that are published to benefit the reader. The posted materials are not copyedited. The contents of all supplementary data are the sole responsibility of the authors. Questions or messages regarding errors should be addressed to the author.

## Notes

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All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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