

Can Chlorhexidine Reduce Bacterial Colonization in Surgical Drains and Surgical Site Infections after Breast Cancer Surgery? A Randomized Controlled Trial.

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ABSTRACT

Background: Breast surgery is considered a clean surgery; however, surgical site infection (SSI) rates are higher than predicted. Postoperative drains remain *in situ* for several days with an inevitable bacterial colonization and increased risk of SSI.

Methods: We conducted a randomized controlled trial from October 2016 to January 2018 in a Mexican cancer center with high SSI prevalence. We included women with elective breast cancer surgery. Patients were randomized to control (standard drain care) or intervention (occlusive dressing with chlorhexidine 2% at the drain exit site). Perioperative management was standardized for both groups. Patient follow-ups were performed on a weekly basis for at least 30 days. Fluid cultures were performed at the 1st and 2nd week as standardized in the laboratory. At the time of drain removal, the inner portion was sectioned and cultured by Maki's semi-quantitative technique. Bacterial quantification was performed using 16 s rRNA-qPCR assay. Culture results of drain fluid and tubing were compared between groups.

Results: We included 104 patients with 167 surgical drains. Patients' clinical characteristics (i.e. age, body mass index, comorbidities, clinical stage, preoperative risk, neoadjuvant therapy) were similar in both groups, with no statistical differences. Bulb fluid cultures at the 1st postoperative week were positive in 42.9% of the control group compared to 27.6% of the antiseptic group ($p=0.04$). Cultures from the 2nd week assessment were positive in 79.7% of the control group vs 53.5% of the antiseptic arm ($p=0.001$). Cultures from drain-tubes were positive in 70.2% and 43.8% ($p=0.001$) of the control and antiseptic group, respectively (Figure 1.) Eleven patients developed an SSI, 3 (5.4%) from the intervention group, and 8 (15.8%) from the control group ($p=0.11$). 84 pathogens were isolated from the control group samples at week 1 vs 52 from the intervention group. *Staphylococcus spp.* were the most commonly found microorganisms in week 1, 61.9% control and 35% intervention group.

Conclusion: Local antiseptics provide an opportunity to test simple, safe, and low-cost interventions that may reduce drain bacterial colonization after breast surgery and potentially decrease infectious complications. Our microbiology findings question breast tissue sterility.

BACKGROUND

Mastectomy is cornerstone for breast cancer treatment. SSI rates reported for this procedure are usually higher than expected for a clean surgery. At Instituto Nacional de Cancerología (INCan) in Mexico City, the frequency of SSI range between 11% and 15% despite several interventions.² Drains are a risk factor for SSI, specially when they remain *in situ* for long periods of time. A few strategies targeted to decrease bacterial colonization of drains have been tested. The use of antiseptics as impregnated dressings or sponges opens new possibilities for the management of drainages and its colonization.

AIMS OF THE STUDY

To determine the frequency of drains' bacterial colonization in patients undergoing breast cancer surgery with the use of impregnated dressings with chlorhexidine gluconate at the drain exit site *versus* the standard of care.

Compare the colonization rates at the first and second postoperative week between groups, and to compare the drain-tip colonization rates between groups.

Determine SSI rates in both groups.

METHODS

Design: Randomized controlled trial, open label.

Population: Patients with breast cancer undergoing mastectomy at INCan between October 1, 2016 and January 31, 2018.

Intervention: Occlusive dressing with chlorhexidine 2% (Tegaderm CHG 10x12 cm, 3M™) at the drain exit site. (Figure 1.)

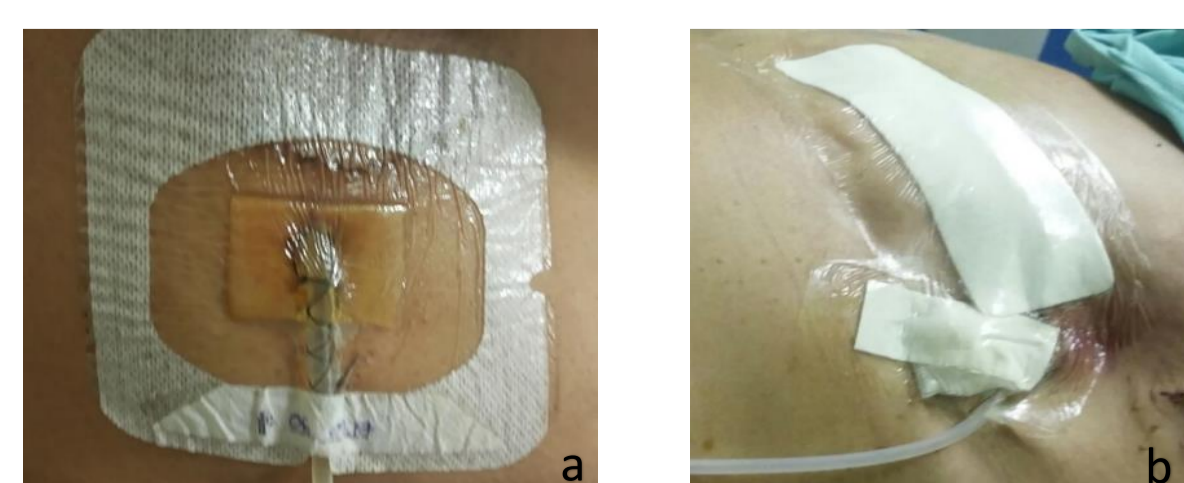


Figure 1. Examples of draping with CHG dressings (a) and the standard of care (b).

Ethical considerations: The study was approved by the Institutional Review Board; *clinicaltrials.gov* NCT03229824.

Selection criteria: Mastectomy with at least one Biovac® drain.

Sample and randomization: 52 patients per arm, stratified by type of surgery (radical vs tumorectomy).

Perioperative standardization: Antimicrobial prophylaxis, skin antiseptics and postoperative wound care.

Surgery and surveillance (Figure 2.)

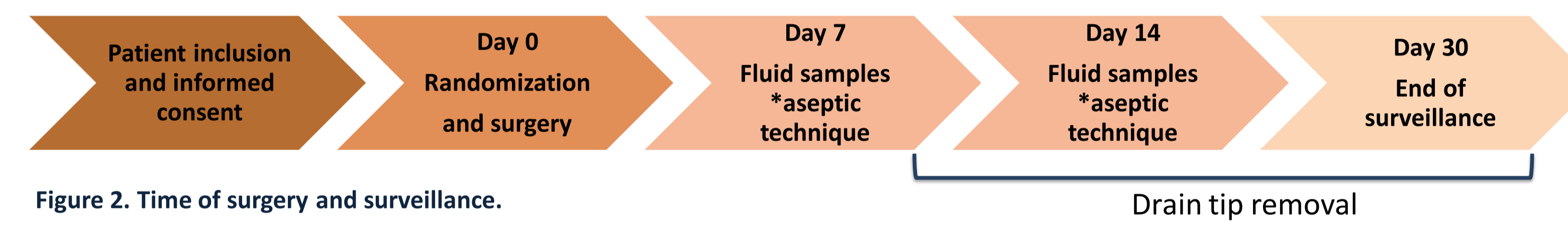


Figure 2. Time of surgery and surveillance.

Microbiology (Figure 3.):

Fluid samples: 7th and 14th day
 Drain tip (<30ml/24 hours)

Colonization cut-off points

>100,000 CFU/ml for fluid samples

>15 CFU/ml for drain-tips



Figure 3. Samples processing.

RESULTS

Table 1. Clinical and demographic characteristics.

	Control n=52	Antisepsis n=52	P value
Age, years (mean, SD)	52±12	55±13	0.30
BMI (%)			
Normal	15 (28.8)	18 (34.6)	0.73
Overweight	21 (40.4)	20 (38.5)	
Obesity	16 (30.8)	14 (26.9)	
Current smoker (%)	9 (17.3)	9 (17.3)	1.00
Diabetes mellitus (%)	9 (17.3)	10 (19.2)	0.80
Clinical stage (%)			
In situ	0	3 (5.8)	0.20
Early	16 (30.7)	11 (21.15)	
Locally advanced	33 (63.4)	38 (73.07)	
Metastatic	3 (5.8)	0	
Hystology (%)			
Ductal	40 (76.4)	39 (75.0)	0.30
Lobular	4 (7.7)	8 (15.4)	
Papillary	0	1 (1.9)	
Mixed	8 (15.4)	4 (7.7)	
Neoadjuvant chemotherapy (%)	25 (48.1)	26 (50)	0.84
Trastuzumab (%)	10 (19.2)	10 (19.2)	1.00

SD, standard deviation. BMI, Body Mass Index.

Table 2. Surgery related variables.

	Control n=54* (%)	Antisepsis n=53* (%)	P value
Surgery (%)			
BCS with/or AND	11 (21.2)	11 (21.2)	1
Radical	41 (78.8)	41 (78.8)	
IRTE (%)	5 (9.2)	2 (3.7)	0.24
Surgical time, min.	130 min	130 min	
median, RIQ	(108-175)	(106-163)	0.30
Bleeding, ml.	100 ml	100 ml	
median, RIQ	(50-150)	(50-150)	0.88
Number of drains [†] n=167 (%)	86 (51.5)	81 (48.5)	
Drain days, median, RIQ	15.5 (12.5-19.25)	15 (13-20.25)	0.53
24-hour volume, ml			
POD 7±1	50 (30-50)	50 (33-73)	0.14
POD 14±1	30 (20-37.5)	25 (20-35)	0.81

*There are more surgical sites than patients because of bilateral procedures.

[†] There are more drains than patients because one surgical site could have one or two drains.

IRTE, Immediate Reconstruction with Tissue Expander.
 BCS, Breast Conservative Surgery. AND, Axillary Node Dissection.
 POD, Postoperative days.

Surgical complications: Eleven patients developed an SSI, 8 (15.8%) in the control group and 3 (5.4%) in the intervention group ($p=0.20$). In 8/11 (72.8%) cases, the pathogen found in the fluid samples and drain tip were the same found in the wound. Seventeen patients (32.7%) developed a non-infectious complication in the control group *versus* 15 patients (28.8%) for the antisepsis group ($p=0.67$).

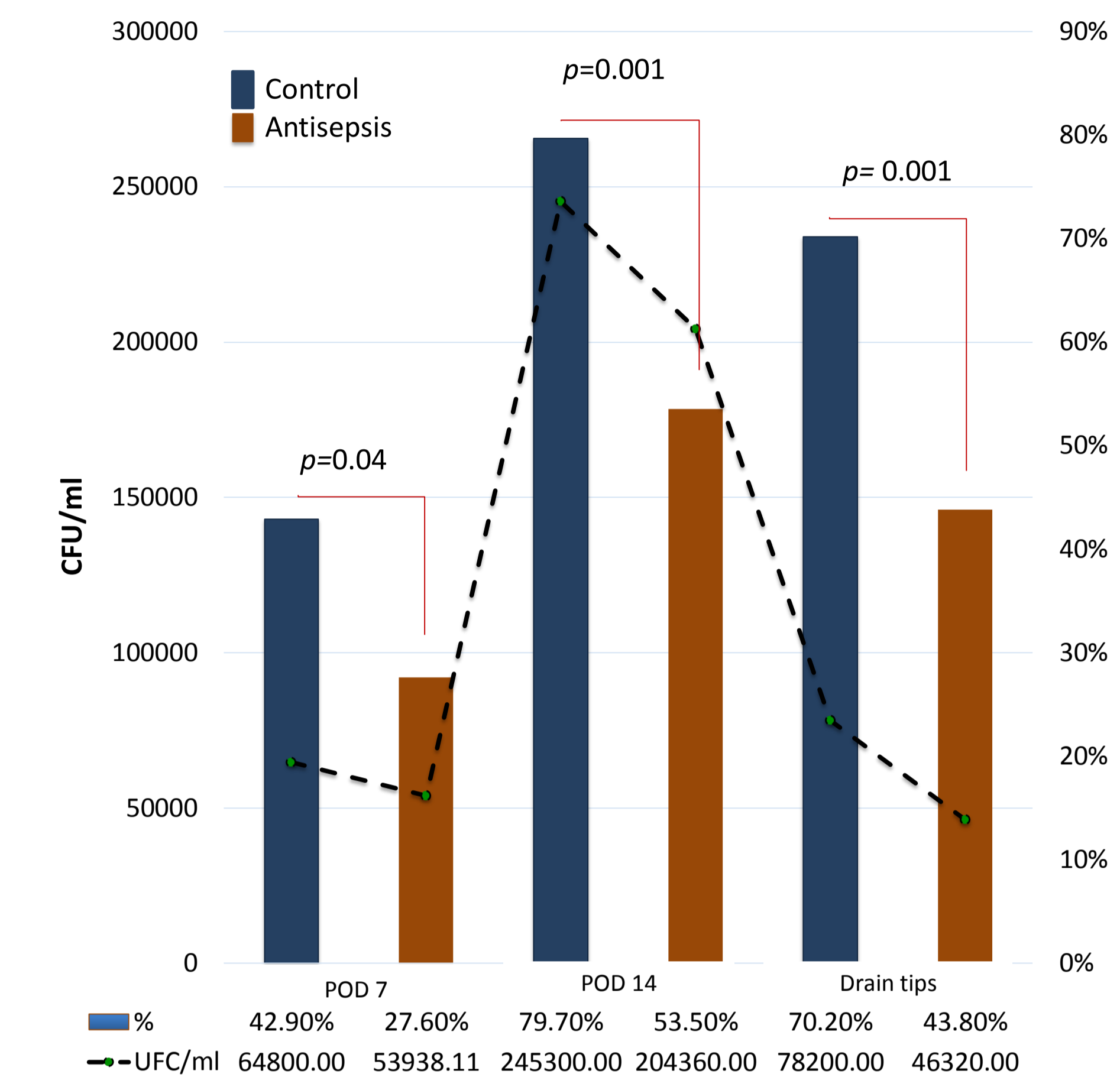


Figure 4. Colonization rates (%) and bacterial load (UFC/ml) in the bulb fluid at the 7th and 14th postoperative day (POD), and in the drain tip at removal.

Table 3. Positive culture results.

Pathogens	Control n=249 (%)	Antisepsis n=146 (%)
7±1 POD	n=72*	n=49*
GPC	53 (73.61)	23 (46.93)
GNB F-	10 (13.88)	10 (20.40)
GNB F+	8 (11.41)	8 (16.32)
GPB	1 (1.38)	3 (6.12)
Fungi	0	3 (6.12)
Anaerobic bacteria	0	2 (4.08)
14±1 POD	n=94*	n=57*
GPC	46 (48.93)	18 (31.57)
GNB F-	17 (18.08)	21 (36.84)
GNB F+	19 (20.21)	12 (21.05)
GPB	7 (7.44)	3 (5.26)
Fungi	3 (3.199)	3 (5.26)
Anaerobic bacteria	2 (2.12)	0
Drain-tip	n=83*	n=40*
GPC	56 (67.47)	28 (70)
GNB F-	2 (2.41)	3 (7.5)
GNB F+	10 (12.05)	6 (15)
GPB	14 (16.87)	3 (7.5)
Fungi	1 (16.87)	0

* Total number of bacteria is different for each sampling day. One sample could have more than one isolation. Percentages were calculated for the total of pathogens per day.

GPC, Gram Positive Cocci. GNB, Gram Negative Bacilli. GPB, Gram Positive Bacilli. F-, Non-fermenting bacilli. F+, fermenting bacilli.

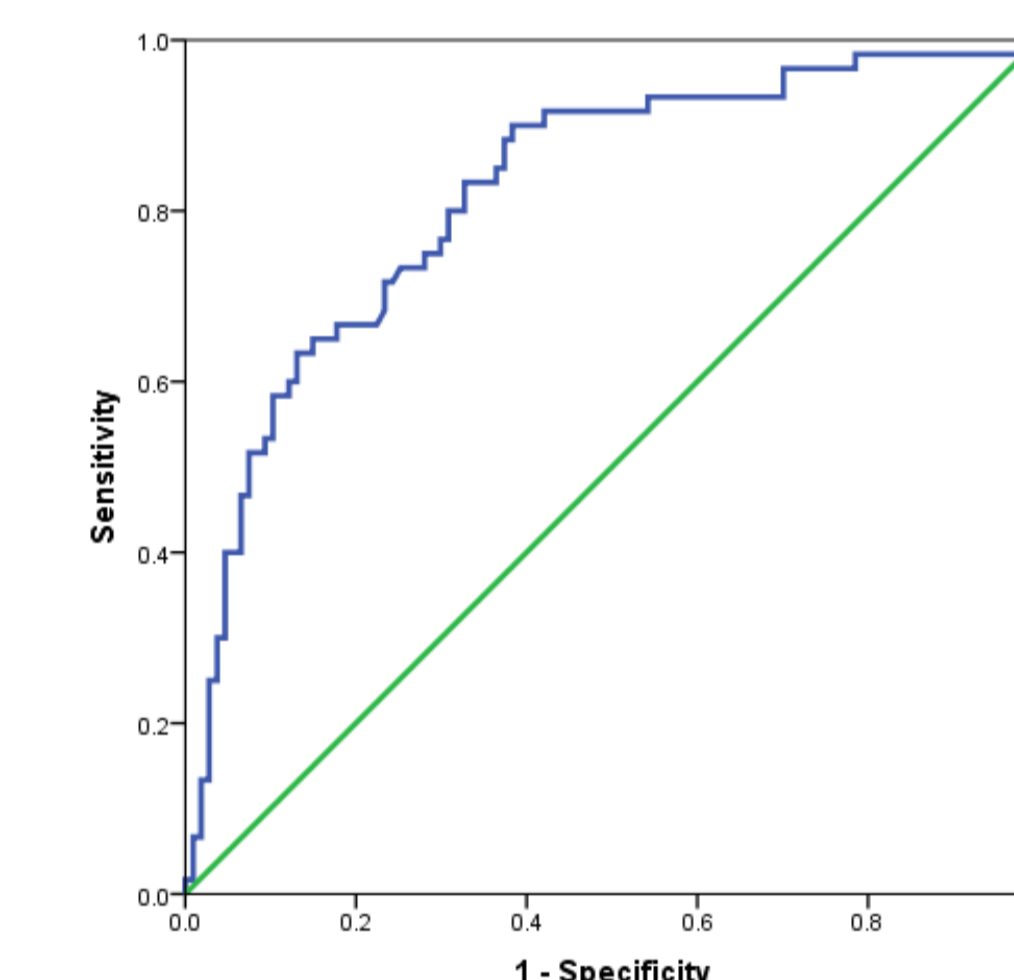


Figure 5. ROC curve for PCR at 7th POD. Sensitivity, specificity, PPV, NPV, LR+ and LR- for bacterial load by qPCR at the 7th POD.

Cut-off point	>40369.0 CFU/ml	
Sensitivity	90.0%	95%CI 79.5-96.2
Specificity	61.7%	95%CI 51.8-70.9
PPV	56.8%	95%CI 46.8-78.9
NPV	91.7%	95%CI 82.6-94.3
LR(+)	2.35	95%CI 1.82-3.03
LR(-)	0.16	95%CI 0.07-0.35

DISCUSSION

The frequency of SSI at INCan is higher than that reported in other oncology series. This study demonstrates that colonization rates of the drainage systems in breast cancer surgery in the first postoperative weeks are high and similar to that reported in other series⁴

We demonstrated that the use of antiseptics at the drain exit site significantly reduced the bacterial colonization of the closed drainage system in breast cancer surgery. The use of absorbent dressings is a maneuver that improves the fixation and the general management of drainages in these procedures. In our trial, SSI rates also decreased by more than 50% in the intervention group, although this was not statistically significant, as sample was not powered to detect this difference. It is necessary to increase the sample in order to find differences about SSI and safely introduce this measure in the usual clinical practice.

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