主　論　文

Title: The effectiveness of hand hygiene depends on the patient's health condition and care environment

Short running Title: Hand hygiene in patients

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ABSTRACT

Aim: We examined how patient hand contamination was associated with underlying disease and treatment environment in order to determine effective hand hygiene methods.

Methods: Samples were collected from inpatients (45 with hematologic malignancies, 48 postoperative), outpatients (48 undergoing hemodialysis, 55 on chemotherapy) and 44 individuals living in nursing homes. All participants provided informed consent for study participation. All subjects performed hand hygiene. Before and after hand hygiene, samples of bacteria were collected from the palm of the hand onto agar media. Bacteria were counted and bacterial strains were identified. We then collected smear samples from the contralateral palm and measured adenosine triphosphate (ATP) levels.

Results: Patient hand contamination was the highest in hemodialysis patients, followed by residents of nursing homes, postoperative patients, patients with cancer receiving chemotherapy, and patients of hematologic malignancies. Regardless of the underlying disease and treatment environment, patients were able to reduce the number of bacterial colonies and ATP by proper hand hygiene. Compared to wet wipes, hand washing seemed to remove bacteria more effectively. MRSA was detected in 30 subjects, none of whom were patients of hematologic malignancies. Of these, 19 tested negative for MRSA after performing proper hand hygiene.

Conclusion: Patient hand contamination is affected by underlying disease and care environment, but can be reduced by encouraging proper hand washing. Patient proper hand hygiene can be reduced MRSA attached on the patient hand, and thus may serve as an effective tool for prevention of healthcare-associated infections.

Key Words: Hand contamination, Hand hygiene, Inpatients, Outpatients, Skin flora of hands

INTRODUCTION

Contact infection is caused by transmission via hands and fingers, which directly contact surfaces in the surroundings. In medical settings, gram-negative bacilli and *Staphylococcus aureus* have been isolated from the hands of health care workers (HCWs) after making direct contact with patients during treatment (Pittet, Dharan, Touveneau, Sauvan, & Perneger, 1999). This suggests that pathogenic microorganisms are present on patient skin as well as in the surrounding environment, and are transmitted via the hands and fingers of HCWs. Therefore, hand hygiene among HCWs has become an effective means to block the route of infection, leading to a reduction in healthcare-associated infection and enhanced patient safety. However, according to a report by the WHO (2009), hand hygiene compliance is still insufficient in both developed and developing countries, with a mean rate of 38.7% (range, 5 - 89%). Moreover, the hands of HCWs were reportedly associated with epidemic outbreaks of healthcare-associated infections (Zawacki, O'Rourke, Potter-Bynoe, Macone, Harbarth, & Goldmann, 2004; Duckro, Blom, Lyle, Weinstein, & Hayden, 2005). In one study that used an experimental model in which nurses checked the pulse of patients whose skin was smeared with gram-negative bacilli, washed their hands with soap and running water, and then touched a urinary catheter, the same bacteria from before hand washing were found on the urinary catheter (Ehrenkranz & Alfonso, 1991). This study suggested the possibility that contact infection could occur even if HCWs performed hand hygiene after contacting patients. Since the development of infection is influenced by the virulence and bacterial load of pathogens, infections might be suppressed by reducing microbial colony counts on the hands of HCWs. In other words, since contact between microbial colonies and the hands of HCWs can be limited by reducing microorganism contamination on the patient side (i.e., source of infection), hand hygiene among patients could represent a strategy for preventing infection. However, given the lack of evidence

regarding microbial contamination of patient hands, hand hygiene among patients has not been established as an effective measure for preventing infection.

A survey of patient hand contamination confirmed that the hands of more than 40% of hospitalized patients were contaminated, and that the degree of hand contamination was higher among patients with limited activity (Kudo, Murakami, Yamaguchi, Suzuki, Hattori, Ishida *et al.*, 1996). Moreover, in patients with paralysis, the hand and fingers on the paralyzed side were more contaminated (Amano, Nakata, Miyoshi, & Fukuta, 2006). Based on these results, it is speculated that the hands of patients with high care dependency are contaminated, and may contribute to the transmission of pathogenic microorganisms. Normal human skin flora varies depending on the area of the body, and according to some reports, the bacterial density is higher in oilier and more moist skin (Reichel, Heisig, & Kampf, 2011), and changes in skin flora and an increase in bacterial count are associated with the duration of hospital stay and morbidity of chronic disease (Larson, Cronquist, Whittier, Lai, Lyle, & Latta, 2000). However, consistent findings have not been reported with regard to the degree of hand contamination among patients, and the degree of patient hand contamination by disease and site of treatment has yet to be demonstrated.

In this study, we examined microbial hand flora and the degree of hand contamination in patients with different underlying diseases and treatment environments to clarify the state of patient hand contamination as a source of contact infection. We also examined associations between patient hand contamination and different diseases as well as treatment environments, and investigated effective hand hygiene methods.

METHODS

1. Design

This study was designed and conducted as a cross-sectional

bacteriological survey.

2. Subjects

Patients with high care dependency requiring assistance in hand hygiene receive medical treatment at hospitals and transitional facilities. Therefore, the present study considered patients in three general hospitals (about 500 beds) and residents of two geriatric health service facilities located near the affiliated university as candidate subjects. Of these, 240 subjects who gave consent (93 inpatients, 103 outpatients, and 44 individuals living in nursing homes) were selected as subjects and divided into five groups as follows: hospitalized patients, divided into patients receiving chemotherapy or acute exacerbation of hematologic malignancies (hereafter, hematologic malignancies group, n=45) and one-day postoperative patients (hereafter, postoperative group, n=48); outpatients, divided into patients undergoing hemodialysis (hereafter, hemodialysis group, n=48) and patients undergoing cancer chemotherapy (hereafter, cancer chemotherapy group, n=55); and residents of nursing homes (hereafter, nursing home group, n=44). Among these, patients in the hematologic malignancies, postoperative, and nursing home groups (n=137) were considered highly dependent on care.

3. Study measures

For hand contamination, bacterial flora and the degree of contamination were examined by collecting specimens from both the right and left palms. Examinations were performed before subjects started their daily activities, and specimens were collected before and after hand hygiene.

Specimen collection and hand hygiene were performed on the bed at 6-7 am before subjects started activities such as face washing (hematologic malignancies and postoperative groups), before treatment was initiated in the outpatient treatment room when subjects visited the hospital (hemodialysis and cancer chemotherapy

groups), or when subjects moved to the day room to have breakfast (nursing home group).

Bacterial flora were collected in the following manner: subjects were asked to touch a hand-shaped agar medium (SCD: Eiken Chemical Co., Ltd.) with the palm of one hand (Figure 1), and the medium was examined by an external contractor (BML, Co., Ltd.) for bacterial quantification and identification. The degree of contamination was assessed by measurements of adenosine triphosphate (ATP) luminescence. For ATP measurements, a swab (LuciPac Pen: Kikkoman Biochemifa Company) was used to wipe the palm and areas between each finger of the other hand, and ATP luminescence was measured using the Lumitester PD-20 (Kikkoman Biochemifa Company) and expressed as relative light units (RLUs) (Figure 2). The Kikkoman Biochemifa Company (2014) recommends measurement of ATP levels in the palms and fingers, with pass and fail levels of 1500 and 3000 RLU, respectively.

4. Hand hygiene methods

The activity status of subjects differed among those who are in bed rest, ambulatory, or wheelchair-dependent. Accordingly, two types of hand hygiene methods were performed. For bed-rest subjects in the hematologic malignancies and postoperative groups, the palm and back of the hands and between each finger were wiped using two pieces of wet tissue (wet wipe group). Ambulatory subjects in the hemodialysis and cancer chemotherapy groups, as well as subjects in the nursing home group who relied on a wheelchair for moving, were asked to wash their hands with liquid soap and running water as usual, and to wipe off their hands with paper towels (hand washing group).

5. Data analysis

The number of colonies and ATP levels collected from the palm before and after hand hygiene practice are presented as mean values for all subjects and each of the five treatment environment groups. The

Wilcoxon signed rank test was used to compare values before and after hand hygiene. The comparison of the degree of hand contamination by treatment environment was performed with Dunnett's multiple comparison test. Rates of decontamination by hand hygiene are shown as changes (%) in ATP by treatment environment and by method of hand hygiene. Regarding identified flora, the number of subjects is shown for each detected bacterial species. As for methicillin-resistant *Staphylococcus aureus* (MRSA), a potential cause of infection, the numbers of MRSA-positive subjects are shown by treatment environment before and after hand hygiene.

6. Ethical considerations

The present study was approved by the ethical review committee of the authors' institution and the ethics boards of the cooperating study facilities. Subjects of this study received written and oral explanations pertaining to the nature and method of this study, that study participation is voluntary, and that they could decline to participate even during the study, with no disadvantage resulting from declining participation. Moreover, we explained that anonymity of data would be maintained strictly, and obtained written consent regarding study participation.

Since the components of the agar medium were attached to the palms of subjects during sample collection, the person in charge of sample collection also assisted subjects with cleaning their hands after the procedure. Moreover, considering that subjects were under medical treatment, assistance was provided in cooperation with nurses in charge of care during data collection when help was requested in their daily lives. Furthermore, arrangements were made to ensure that in the event of an unexpected occurrence, the patient's attending physician could be contacted to address any issues.

RESULTS

In all 240 subjects, the number of colonies significantly

decreased from 382.6 before hand hygiene to 180.7 after hand hygiene (P = .000). The RLU of ATP also significantly decreased from 6914.1 before to 2269.8 after hand hygiene (P = .012) (Figure 3). The comparison of the number of colonies before and after hand hygiene by treatment environment revealed a significant decrease in all groups after hand hygiene, from 210.0 to 70.9 in the hematologic malignancies group, 407.3 to 154.8 in the postoperative group, 365.5 to 123.1 in the hemodialysis group, 265.6 to 140.4 in the cancer chemotherapy group, and 704.1 to 434.0 in the nursing home group (P = .000). ATP was also clearly decreased in all treatment environments after hand hygiene, compared to before (P = .000) (Figure 4).

Among the five treatment environment groups, the nursing home group had the highest number of colonies before hand hygiene, and the number of colonies in this group was significantly higher than that of the hematologic malignancies group or cancer chemotherapy group (P < .05). Compared to the other four treatment environment groups, the nursing home group had a significantly higher number of colonies even after hand hygiene (P < .05). The hemodialysis and nursing home groups both showed high ATP values before hand hygiene. Before hand hygiene, ATP values in the nursing home group were significantly higher than those in the hematologic malignancies group, the letter of which showed the lowest ATP values (P < 0.05). No significant changes were observed after hand hygiene in all groups (Table 1).

Before hand hygiene, *Staphylococcus epidermidis* was detected from the majority of subjects, as well as *Pseudomonas* and *Acinetobacter*, which are naturally resistant bacteria. *S. aureus* was detected in 44 subjects, of whom 29 (66%) had MRSA (Table 2). The breakdown of the 29 MRSA-positive subjects by treatment environment was as follows: 0 in the hematologic malignancies group, 9 in the postoperative group, 5 in the hemodialysis group, 5 in the cancer chemotherapy group, and 10 in the nursing home group. Of the 29 MRSA-positive subjects, 11 were still positive for MRSA after hand

hygiene (Table 3).

The efficacy of the two hand hygiene methods were compared with regard to their rate of decontamination (ATP levels). These rates were 45.3% in the wet wipe group and 73.9% in the hand washing group (Table 4). In the hematologic malignancies and postoperative groups, the rates of decontamination with wet wipes were 49.5% and 43.4%, respectively. In the hemodialysis, cancer chemotherapy, and nursing home groups, the rates of decontamination after hand washing were 86.8%, 58.8%, and 61.7%, respectively (Table 5).

DISCUSSION

In the present study, the hands and fingers of all subjects were contaminated, although the degree of contamination varied by disease and treatment environment.

A previous study on patient hand contamination found that the hands and fingers of 39% of hospitalized patients were contaminated with more than one type of pathogenic microorganism, and the degree of hand contamination tended to increase with prolongation of hospital stay (Istenes, Bingham, Hazelett, Fleming, & Kirk, 2013). Moreover, patients with high care dependency who cannot practice hand hygiene on a frequent basis showed a higher degree of hand contamination (Okada & Fukai, 2006). These patients require care providers to perform hand hygiene for them, and in many hospitals, nurses—who visit the patient room most frequently and stay in the room for a long time—play this role (Cohen, Hyman, Rosenberg, & Larson, 2012). However, nurses have indicated that thorough implementation of hand hygiene has not been achieved, although they understand the importance of patient hand hygiene (Okada, Yamamizu, & Fukai, 2013). Moreover, nurses feel that their own hand hygiene behaviors may not be appropriate, though they have been educated on infection prevention (Burnett, 2009). If a nurse provides care for a patient with contaminated fingers or hands, and then provides care to a different patient without first implementing the appropriate hand washing, this

could easily lead to hand contamination. Thus, nurses as care providers must improve their own hand hygiene behaviors, and promoting hand washing among patients in order to reduce patient hand contamination. These will enhance infection prevention control.

When compared by treatment environment, patients with hematologic malignancies and those with cancer undergoing outpatient chemotherapy had the lowest number of colonies and ATP. Moreover, after hand hygiene, these two patient groups achieved a reduction in ATP to ≦1,500 RLU, which is the reference value recommended by the Kikkoman Biochemifa Company (2014). Both of these groups have some risk of infection due to leucopenia associated with anti-cancer drugs. Compliance rates for hand and finger hygiene is reportedly high in hematology departments (Costa, Neves, Marra, Camargo, Cardoso, Victor *et al.*, 2013), and it is likely that the awareness of infection risk is high. Outpatients undergoing chemotherapy also tend to have a relatively high self-care capacity (Saito, & Sato, 2010), and it is thought that ATP and bacterial counts were lowered by everyday infection prevention activities such as hand hygiene. On the other hand, patients undergoing dialysis showed high values of ATP before hand hygiene. More than 40% of dialysis patients complain of moderate or worse itching sensation (Pisoni, Wikstrom, Elder, Akizawa, Asano, Keen *et al.*, 2006), and their skin of the forearm, where the blood access is constructed, is weakened due to repeated puncture over a long period of time. The skin is thus more susceptible to bacterial colonization (Rocha, Ferreira de Almeida E Borges, & Gontijo Filho, 2009), and the level of contamination with colonizing bacteria such as *S. aureus* and gram-negative bacillus is likely increased. Facility residents also had high ATP values and high colony counts before hand hygiene. Many facility residents were wheelchair users, and were unable to wash their hands unaided. It was essential for care workers to provide the necessary support in maintaining residents of hand hygiene. O'Donnell *et al.* (2015) also reported that facility residents are sometimes deterred from hand

hygiene practices due to difficulties in accessing the hand washing area or using the hand sanitizers, which also opens the door for reduced compliance for hand hygiene. In fact, a higher detection rate of pathogenic microorganisms has been reported for patients who cannot go to a hand-wash station by themselves compared to other patients (Istenes *et al.*, 2013). Meanwhile, the dialysis group had the highest rate of decontamination after hand hygiene. Although the present study did not unify the procedure or duration of hand washing, dialysis patients tended to perform long and extensive hand hygiene, including the forearm where the puncture site is located, immediately before starting dialysis. The longer the time spent rubbing the hands with soap and rinsing with running water, the higher the virus removing effect (Mori, Hayashi, Noguchi, Kai, Ohe, Sakai *et al.*, 2006). Presumably, thorough hand hygiene to remove contamination has been implemented among dialysis patients. Taken together, our findings show that the degree of hand and finger contamination varies by disease and treatment environment. That is, the degree of hand and finger contamination is influenced by underlying disease and treatment environment.

The present study detected *Staphylococcus epidermidis*, a *coagulase-negative staphylococci* (CNS) that lives on the human skin, in 99% of the subjects. It has been treated as a contaminant due to its weak pathogenecity, yet roughly 70% of CNS detected in blood cultures are drug-resistant strains with methicillin resistance (MR-CNS) (Oshitani, Ishikawa, Murata, Aoyagi, Yabe, & Aoshima, 2011; Kawaguchi, Minamide, Mori, & Igimi, 1997). MR-CNS has been recognized as an important pathogenic bacterium that causes intravascular catheter-related infection and infective endocarditis in immunocompromised patients (Gardlund, Bitkover, & Vaage, 2002; Pfaller & Herwaldt, 1988; Oppenheim, 1998). CNS and *S. aureus* produce a capsule polysaccharide that enables them to stick easily to the catheter surfaces and create a biofilm, making it difficult to decontaminate using antimicrobial agents. As such, it is necessary to

decrease continuously the number of resident microbiota on the skin where the vascular catheter is inserted, and patients must maintain daily hand hygiene as well as disinfection at the time of catheter insertion. In the present study, we also isolated from the hands and fingers some naturally resistant *Pseudomonas* and *Acinetobacter,* which can cause respiratory tract infections and urinary tract infections. These are often identified in hospital environments, and are known as microbes that can easily establish themselves on patients who are receiving antibiotics or immunosuppressants. In addition, patients in long-term acute care facilities show a fairly high carriage rate (30%) for *Acinetobacter* (Furuno, Hebden, Standiford, Perencevich, Miller, Moore *et al.*, 2008). Hand and finger contamination represents a risk factor for opportunistic infection among elderly in long-term acute care facilities and those undergoing treatment, so patient hand hygiene is important. If HCWs wear the specialized gloves (Ng, Teh, Ng, Eng, & Tan, 2011; Ginny Moore, Dunnill, & Wilson, 2013) made to protect one from MRSA acquisition, contact infections could be prevented. However, roughly half of HCWs use gloves inappropriately, and contact infection prevention is not yet sufficient (Loveday, Lynam, Singleton, & Wilson, 2014). Therefore, by eliminating even slightly the number of disease-causing bacteria established on the patients will lead to a reduction in inoculum size.

In recent years, MRSA has been on the decline due to enhanced hospital infection control. Still, MRSA makes up 50-70% of *S. aureus* isolated from inpatients (JANIS, 2011), and 10-30% of that isolated from outpatients (Yamaguchi, Nakamura, Chiba, & Matsumoto, 2012). Although no difference was observed in the detection rate of MRSA between inpatients and outpatients in the present study, 66% of isolated *S. aureus* strains were MRSA, and 12% of the subjects were MRSA-positive. MRSA is a bacterium present in the human oral cavity, skin, and gastrointestinal tract, and causes infections such as cystitis, endocarditis, vascular catheter infection, and soft tissue infection of the skin. The ratio of MRSA isolates is especially high among dialysis

patients, and hospitalization related to MRSA is reportedly linked with a high mortality rate (17%) (CDC, 2007). Moreover, cancer patients who have undergone chemotherapy are at an increased risk of carrying MRSA (Schaefer, McMullen, Mayfield, Richmond, Warren, & Dubberke, 2009), and at long-term care facilities where roughly 5% of residents are colonized with MRSA, group infections have become an issue (Pfingsten-Wurzburg, Pieper, Bautsch, & Probst-Kepper, 2011; Ibrahem, Salmenlinna, Virolainen, Kerttula, Lyytikainen, Jagerroos *et al.*, 2009). Patients colonized with MRSA are often detected MRSA on the skin or in their environment (Chang, Sethi, Stiefel, Cadnum, & Donskey, 2010), and this bacterium is a cause of postoperative infection (Huang, & Platt, 2003; Milstone, Goldner, Ross, Shepard, Carroll, & Perl, 2011). As such, the "Clinical practice guidelines for antimicrobial prophylaxis in surgery" (Bratzler, Dellinger, Olsen, Perl, Auwaerter, Bolon *et al.*, 2013) recommend prophylactic administration of antibiotics and skin sanitization. In other words, HCWs should take responsibility for the removal of MRSA and other naturally resistant bacteria that are on the hands of the patient, and it should be considered as a preventative measure against healthcare-associated infections.

As hand hygiene, which can be performed in various ways, can reduce hand contamination and the number of colonies by hand hygiene, MRSA-positive patients decreased after implementation of hand hygiene. The incidence of infection, however, has been reported to decrease with implementation of a hand hygiene program among HCWs as well as residents in a long-term care facility (Schweon, Edmonds, Kirk, Rowland, & Acosta, 2013). Implementation of active hand hygiene practice among patients could help eliminate a source of infection via contact. Also, when ATP was measured as an indicator of contamination level, the rate of decontamination was higher in the hand washing group than in the wet tissue group. Mori *et al.* (2007) found that hand washing with soap and running water effectively removes viruses, and although wet tissues are useful, its effects on

virus removal varies depending on the materials it comprises. Hand washing with soap and running water, which was also shown to be effective in the present study, is thus considered an ideal hand hygiene method for patients. However, in the present study, an alcohol-based disinfectant, which is the number one hand hygiene choice among HCWs, was not included in the comparison. Since hand disinfectants are convenient for hand hygiene, their effectiveness should be verified in a future study.

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Conflict of Interest

All authors declare that they have no competing interests.

Author contributions

J.O. was responsible for research concept and design, acquisition of subjects and data, analysis and interpretation of data, and manuscript preparation. Y.Y. collected the data. K. F. proposed conducting this study. All authors contributed to the writing of the manuscript. All authors approved the final version of the manuscript.

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A

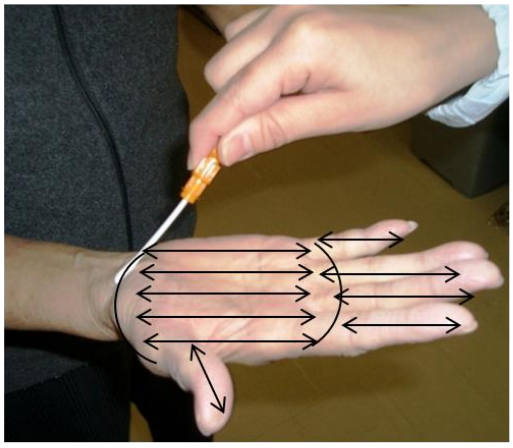
B

Figure 1. Methods of bacterial sampling using a hand-shaped agar medium

A: Sampling method for inpatients.

B: Sampling method for outpatients and nursing home residents.

A



B

Figure 2. Method of bacterial sampling by a swab test

A: The palm and areas between each finger were wiped using a swab.
B: LuciPac Pen® (L) and Lumitester PD-20® (R).

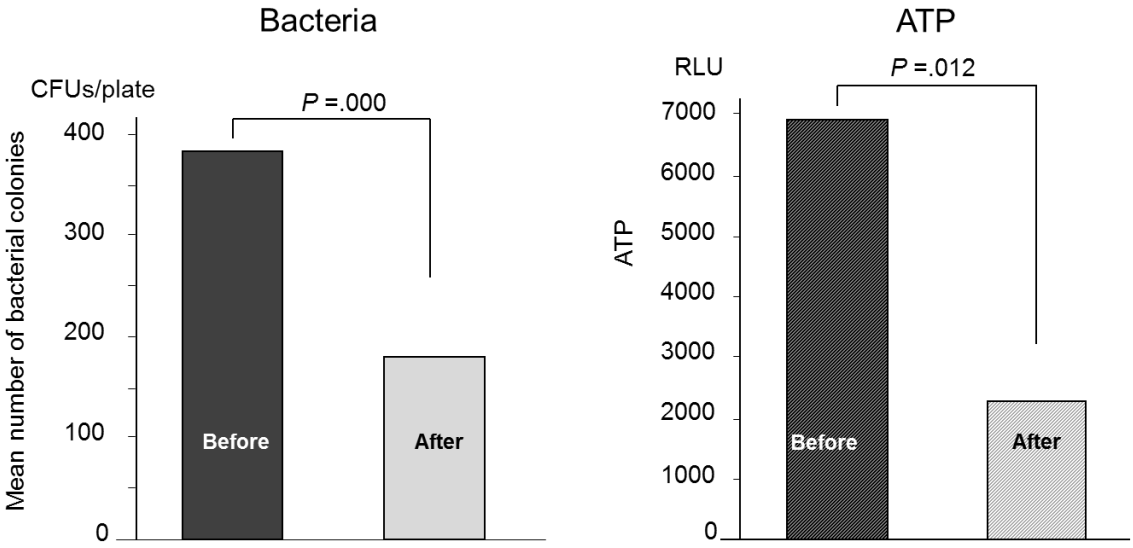


Figure 3. Mean number of bacterial colonies and ATP levels before and after hand hygiene in all subjects (n = 240)

Wilcoxon signed rank test.

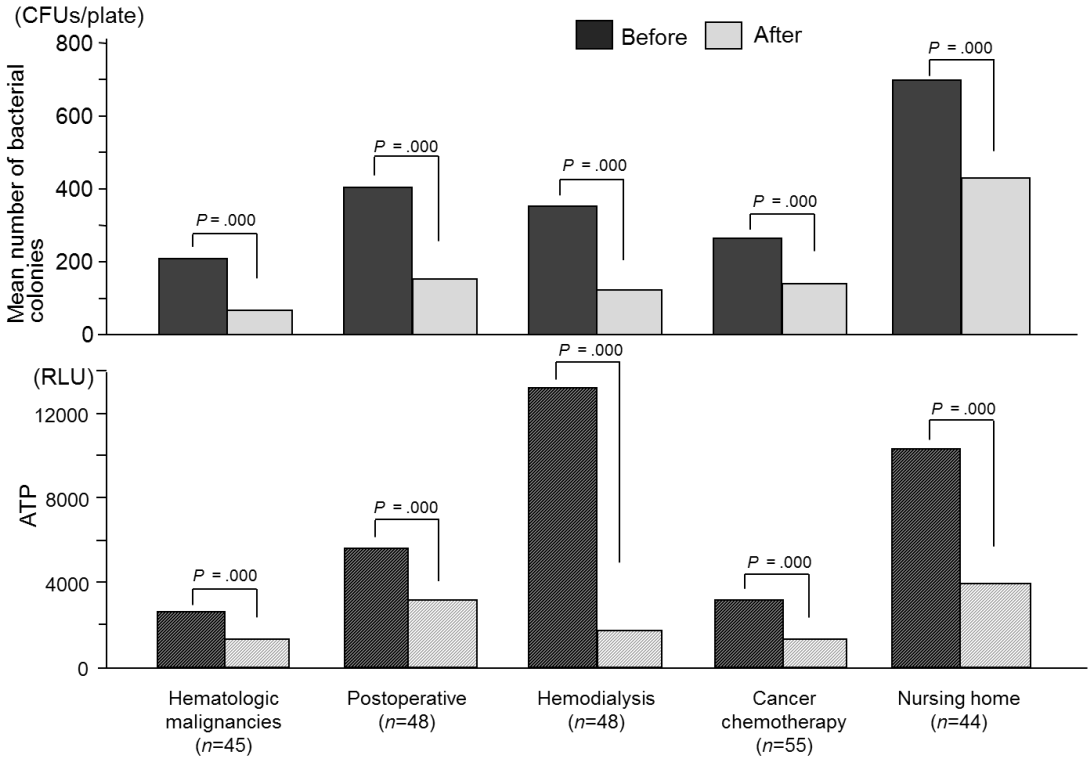


Figure 4. The comparison of hand contamination before and after hand hygiene by treatment environment.

Wilcoxon signed rank test.

Table 1. Hand contamination before and after hand hygiene by treatment environment

Subjects	Bacterial colonies (CFUs/plate)		ATP levels (RLU)	
	Before	After	Before	After
Inpatients				
Hematologic malignancies (*n*=45)	210.0	70.9	2616.2	1320.6
Postoperative (*n*=48)	407.3	154.8	5640.6	3189.8
Outpatients				
Hemodialysis (*n*=48)	356.6	123.6	13263.7	1752.0
Cancer chemotherapy (*n*=55)	267.5	140.3	3202.6	1320.4
Residents				
Nursing home (*n*=44)	704.1	434.0	10411.7	3988.5

Dunnett test due to non-parametric distribution of variables. * $P < .05$

Table 2. Bacterial species detected on the palm before hand hygiene

Category	Inpatient		Outpatient		Residents
	Hematologic malignancies (*n*=45)	Postoperative (*n*=48)	Hemodialysis (*n*=48)	Cancer chemotherapy (*n*=55)	Nursing home (*n*=44)
Staphylococcus epidermidis	43	48	48	54	44
Staphylococcus aureus	0	13	11	5	15
MRSA	0	9	5	5	10
Streptococcus	6	5	1	1	0
Corynebacterium	18	20	36	36	31
Bacillus	27	28	43	50	35
Pseudomonas	25	25	44	44	33
Acinetobacter	4	5	9	15	19
Escherichia coli	1	0	1	0	0
Fungi (yeast, hypha)	5	0	4	4	8

MRSA: Methicillin-resistant *Staphylococcus aureus*

Table 3. Changes in the number of MRSA-positive patients before and after hand hygiene by treatment environment

Subjects	Before hand hygiene MRSA(+)	After hand hygiene MRSA(+)
Hematologic malignancies (*n*=45)	0	0
Postoperative (*n*=48)	9	4
Hemodialysis (*n*=48)	5	2
Cancer chemotherapy (*n*=55)	5	1
Nursing home (*n*=44)	10	4
Total (*n*=240)	29	11

MRSA : Methicillin-resistant *Staphylococcus aureus*

Table 4. Comparison of hand decontamination rates by hand hygiene method

Hand hygiene	ATP levels
Wet wipe (*n*=93)	45.3%
Hand washing (*n*=147)	73.9%

Table 5. Comparison of hand decontamination rates by treatment environment

Subjects	ATP levels
Hematologic malignancies (*n*=45)	49.5%
Postoperative (*n*=48)	43.4%
Hemodialysis (*n*=48)	86.8%
Cancer chemotherapy (*n*=55)	58.8%
Nursing home (*n*=44)	61.7%