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# 단일 3차 의료기관에 내원한 당뇨병성 족부병변 환자의 창상 배양검사를 통한 세균 검출 현황

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# The Current Status of Bacterial Identification by Wound Culture for Diabetic Foot Lesions in a Single Tertiary Hospital in South Korea

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**Purpose:** The present study aimed to develop guidelines regarding initial choice of antibiotics for diabetic foot ulcers (DFU) by investigating bacterial isolates.

**Materials and Methods:** This study included 223 DFU patients that visited a single tertiary hospital and underwent bacterial culture between January 2016 and February 2020. The study was conducted in two parts: 1) to compare bacterial isolates and wound healing according to comorbidities such as chronic kidney disease (CKD) and peripheral artery disease (PAD), and 2) to compare bacterial isolates according to wound depth using the Wagner classification.

**Results:** Of the 223 patients, 43 had CKD (group A), 56 had PAD (group B), 30 had CKD and PAD (group C), and 94 had none of these comorbidities (group D). The isolation rate for multidrug-resistant gram-negative bacteria (MRGNB) and gram-negative to gram-positive bacteria ratio were highest in group C (p=0.018, p=0.038), and the proportion that achieved wound healing was lowest in group C (p<0.001). In the second part of the study, subjects were classified into 5 grades by wound depth using the Wagner classification; 13 grade I, 62 grade II, 60 grade III, 70 grade IV, and 17 grade V. No significant difference was observed between these grades in terms of isolation rates or gram-negative to gram-positive bacteria ratios.

**Conclusion:** This study suggests antibiotics that cover gram-negative bacteria including MRGNB produces better results in the presence of CKD and PAD and that initial antibiotic choice should be based on the presence of CKD and PAD rather than wound depth.

**Key Words:** Diabetic foot ulcer, Bacterial culture, Wagner grade, Resistant bacteria, Antibiotics

## INTRODUCTION

As diabetes prevalence is increasing annually, diabetic foot ulcer (DFU) occurs in approximately 15% of patients with diabetes and infection is usually accompanied with DFU, therefore antibiotic treatment is often required.[1] Since the need for admission care is inevitable in most patients associated with infection, the economic burden of medical expenses is growing annually.[2] In patients with diabetes, since immunity weakens with decreased function of neutrophil, soft tissue infections can worsen quickly and may be associated with osteomyelitis and sepsis without adequate antibiotic therapy.[3] Recent studies have reported that antibiotic-resistant bacteria in patients with DFU are becoming

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increasingly prevalent.[4,5] The use of high-end antibiotics is difficult in primary care and small-scale clinics because it is restricted by health insurance regulations.

Diabetes is considered as a strong risk factor for chronic kidney disease (CKD), and DFU associated with CKD has also been reported to affect the need for lower-extremity amputation in diabetic patients.[6-8] Furthermore, CKD is known as an independent risk factor for the development of peripheral artery disease (PAD).[9] PAD is currently estimated to be present in more than half the patients with DFU. And presence of PAD is associated with increased risk of non-healing ulcers, infection and major limb amputation as well as an elevated risk of cardiovascular morbidity and overall mortality. For this reason, PAD has gained much attention as a prognosis of DFU patients.[10,11] Therefore, the comorbidity of CKD and PAD is a critical factor to be considered in the treatment of DFU patients and collaborative care with a multidisciplinary approach is crucial. However, in primary care clinics, prompt management and appropriate antibiotic selection at the beginning of symptom onset have not frequently been performed. Our institution has treated DFU through interdisciplinary and integrated care in the diabetic foot center (orthopedics, endocrinology, cardiology, infectious diseases, and radiology). This study aimed to facilitate the selection of empirical antibiotics for DFU by comparing bacterial isolates and wound healing according to presence of comorbidities such as CKD and PAD, and by comparing bacterial isolates according to wound depth by Wagner classification.[12]

## MATERIALS AND METHODS

### 1. Patients

#### 1) Data collection and ethics approval

This study retrospectively reviewed 223 DFU patients who underwent bacterial culture tests at the initial visit of the diabetic foot center and had accurate diagnosis code on electric medical records in our hospital between January 2016 and February 2020 and proceeded after receiving written informed consent from all of patients. This study was performed after gaining IRB approval from investigators' institution (DAUHIRB-21-009).

#### 2) Bacterial culture

Bacterial culture tests for DFU were performed on the first day of visit to our diabetic foot center before antibiotic administration. Bacterial cultures were harvested from the deep tissue of DFU after being sterilized with alcohol and betadine. Bacterial identification, and antibiotic susceptibility tests were carried out. The results of bacterial identification were classified as usual pathogens on the basis of the International Working Group on the Diabetic Foot (IWGDF)

**Table 1.** International Working Group on the Diabetic Foot (IWGDF) 2019 Update Guideline

| Infection severity | Additional factor | Usual pathogen | Potential empirical regimen |
|---|---|---|---|
| Mild | No complicating features | Gram-positive cocci | S-S pen<br>First generation cephalosporin |
| | β-lactam allergy or intolerance | Gram-positive cocci | Clindamycin; fluoroquinolone; T/S; macrolide; doxycycline |
| | Recent antibiotic exposure | Gram-positive cocci +gram-negative rod | Amoxicillin/Clavulanate; ampicillin/Sulbactam; fluoroquinolone; T/S |
| | High risk for MRSA | MRSA | Linezolid; T/S; doxycycline; macrolide |
| Moderate or severe | No complicating features | Gram-positive cocci ±gram-negative rod | Amoxicillin/clavulanate; ampicillin/sulbactam, second/third generation cephalosporin |
| | Recent antibiotics | Gram-positive cocci ±gram-negative rod | Ticarcillin/clavulanate; piperacillin/tazobactam; third generation cephalosporin; group 1 carbapenem |
| | Macerated ulcer or warm climate | Gram-negative rod including *Pseudomonas* | Ticarcillin/clavulanate; piperacillin/tazobactam; S-S pen+ceftazidime; S-S pen+ciprofloxacin; group 2 carbapenem |
| | Ischemic limb/necrosis/gas forming | Gram-positive cocci ±gram-negative rod±anaerobes | Second/third generation cephalosporin+clindamycin or metronidazole |
| | MRSA risk factors | MRSA | Consider adding, or substituting with, glycopeptides; linezolid; daptomycin; T/S (±rifampin); doxycycline |
| | Risk factors for resistant gram-negative rod | Extended-spectrum β-lactamase-producing organism | Carbapenems; fluoroquinolone; aminoglycoside and colistin |

MRSA: methicillin-resistant *Staphylococcus aureus*, S-S pen: semisynthetic penicillinase-resistant penicillin, T/S: trimethoprim-sulfamethoxazole.

2019 update guideline on the diagnosis and treatment of foot infection in persons with diabetes (Table 1). According to IWGDF, many studies demonstrated that the most common pathogen in infection of diabetic foot is *Staphylococcus aureus*. And many studies about patients in Asia showed that aerobic gram-negative bacilli are often isolated either alone or in combination with gram-positivie cocci and often resistant to multiple commonly used antibiotics. Based on this studies, we classified bacterial isolates into methicillin-sensitive *Staphylococcus aureus* (MSSA), methicillin-resistant *Staphylococcus aureus* (MRSA), multidrug-resistant gram-negative bacteria (MRGNB), and extended spectrum beta-lactamase (ESBL)-producing bacteria. MRGNB included ESBL-producing bacteria, multidrug resistant *Pseudomonas aeruginosa* and multidrug resistant *Acinetobacter baumannii*. Although when result of bacterial culture shows no growth of bacteria, biofilm formed by multibacterial colonization could be confounders,[13] in clinical practice, because we have to select antibiotics according to that result, we could not help but regard result of no growth in bacterial culture as an absence of bacterial in this study.

#### 3) Treatment

At first visit, wound cultures were obtained before administration of empirical intravenous antibiotics. Then, intravenous antibiotics were selected according to the results of bacterial culture. All patients diagnosed with PAD on computed tomography angiography underwent percutaneous transluminal angioplasty (PTA). Of those, patients on dialysis with CKD underwent dialysis immediately after PTA. In patients with CKD but not on dialysis, appropriate hydration and *N*-acetylcysteine were administered before and after PTA. Wound debridement was done for patients with residual wound infection or necrotic tissue after PTA and taking time to fully demarcate.

### 2. Comparisons of bacterial isolates and the ratio of wound healing to amputation of patients according to presence of comorbidities

The patients were classified into four groups according to comorbidities: 1) patients associated with CKD (group A); 2) patients associated with PAD (group B); 3) patients associated with both CKD and PAD; and 4) patients associated with none of the conditions (group D). PAD was diagnosed when ankle-brachial index was less than 0.9 in the affected side or lesions were clearly seen in computed tomography angiography of lower limbs. CKD was diagnosed when glomerular filtration rate was less than 60 mL/min/1.73 $m^2$. Bacterial the isolation rates and the ratio of wound healing were compared among groups. The ratio of wound healing was judged through comparison with the ratio of patients who have simply performed any kinds of amputations. And the ratio of isolation rates of gram-negative to gram-positive bacteria was compared among groups because most physicians empirically prescribe the antibacterial coverage of only gram positive bacteria and the anaerobes, we thought that comparing the isolation rates of gram-negative to gram-positive bacteria could be an initial consideration in antibiotics selection.

### 3. Comparisons of bacterial isolates according to wound depth by Wagner classification

Wound depth was graded according to the Wagner classification system (Table 2). Bacterial isolation rates and the ratio of isolation rates of gram-negative to gram-positive bacteria were compared among grades.

### 4. Statistical analysis

All statistical analyses were performed using IBM SPSS ver. 22.0 (IBM Corp., Armonk, NY, USA). The isolation rates for gram-positive bacteria, gram-negative bacteria, non-isolation rate, MSSA, MRSA, MRGNB, and ESBL-producing bacteria were obtained in each group. Chi-square test was used to compare the isolation ratio of gram-negative to gram-positive bacteria among groups according to the presence

**Table 2.** Wagner Classification of Diabetic Foot Ulcers

| Grade | Denomination | Description |
|---|---|---|
| 0 | Foot at risk | Thick calluses, bone deformities, clawed toes, and prominent metatarsal heads |
| I | Superficial ulcers | Total destruction of the thickness of the skin |
| II | Deep ulcers | Penetrates through skin, fat and ligaments, but not affect bone |
| III | Abscessed deep ulcers | Limited necrosis in toes or the foot |
| IV | Limited gangrene | Localized gangrene |
| V | Extensive gangrene | Necrosis of the complete foot, with systemic effects |

of comorbidities and the ratio of isolation rates of gram-negative to gram-positive bacteria among grades according to Wagner classification. Additionally, Fisher's exact test was used to test differences in the isolation rates of bacteria and the ratio of wound healing between groups according to the presence of comorbidities and the isolation rates of bacteria among grades according to Wagner classification. Differences were considered statistically significant at $p<0.05$.

# RESULTS

## 1. Demographics

Of all 223 DFU patients, gram-positive bacteria were cultured from 85 (38.1%) patients and gram-negative bacteria from 122 (54.7%). The mean age was 66 years (34~99 years), and 168 (75.3%) male and 55 (24.7%) female. A total of 223 patients were divided into four groups consisting of 43 (19.3%) in the group A, 56 (25.1%) in the group B, 30 (13.4%) in the group C, and 94 (42.1%) in the group D. The average Wagner grade was 3.07±1.06. Grade according to wound depth was grade I in 13 (5.8%) patients, grade II in 62 (27.8%), grade III in 60 (26.9%), grade IV in 70 (31.4%), and grade V in 17 (7.6%) (Table 3).

## 2. Results of bacterial identification

Of all 223 patients, gram-positive bacteria were detected in 85 (38.1%) patients, gram-negative bacteria in 122 (54.7%), and no isolation in 36 (16.1%). There were 41 (18.4%) patients having more than two species of bacteria coexisting, and 20 (8.9%) having both gram-positive and gram-negative bacteria. Among gram-positive bacteria, MRSA was detected from 32 (14.3%) patients and MSSA from 19 (8.5%). MRGNB were detected in 28 (12.6%) patients. Of these multidrug-resistant gram-negative bacteria, multidrug-resistant *P. aeruginosa* was isolated from 3 (1.3%) patients, multidrug-resistant *A. baumannii* from 4 (1.8%), and ESBL-producing bacteria from 22 (9.9%) (Table 4).

**Table 3.** Demographic Characteristics of Diabetic Foot Ulcer Patients

| Variable | Value |
|---|---|
| Age (yr) | 66 (34~99) |
| Sex | |
| Male | 168 (75.3) |
| Female | 55 (24.7) |
| Comorbidities | |
| CKD | 43 (19.3) |
| PAD | 56 (25.1) |
| CKD+PAD | 30 (13.4) |
| No CKD & PAD | 94 (42.1) |
| Wagner grade | |
| I | 13 (5.8) |
| II | 62 (27.8) |
| III | 60 (26.9) |
| IV | 70 (31.4) |
| V | 17 (7.6) |

Values are presented as mean (range) or number (%).
CKD: chronic kidney disease, PAD: peripheral artery disease.

## 3. Correlation of bacterial isolates and the ratio of wound healing with the presence of comorbidities

There were no statistical significance in differences of the isolation rate of gram-positive and gram-negative bacteria and the non-isolation rate of bacteria among groups according to the presence of comorbidities (Fig. 1). In the isolation rates of MSSA, MRSA, MRGNB, and ESBL-producing bacteria, there was a statistical significant difference only in MRGNB among groups ($p=0.018$; Table 5, Fig. 2). And there was statistical significance in the isolation ratio of gram-negative to

**Table 4.** Bacterial Species Cultured from Diabetic Foot Ulcer

| Variable | Value |
|---|---|
| Gram-positive bacteria | 85 (38.1) |
| Methicilin-sensitive *Staphylococcus aureus* | 19 (8.5) |
| Methicilin-resistant *Staphylococcus aureus* | 32 (14.3) |
| *Streptococcus agalactiae* | 11 (4.9) |
| *Streptococcus dysgalactiae* | 7 (3.1) |
| Methicilin-sensitive coagulase-negative *Streptococcus* | 9 (4.0) |
| Methicilin-resistant coagulase-negative *Streptococcus* | 16 (7.2) |
| *Enterococcus faecalis* | 8 (3.6) |
| *Enterobacter cloacae* | 8 (3.6) |
| Others | 4 (1.8) |
| Gram-negative bacteria | 122 (54.7) |
| Extended spectrum beta-lactamase producing bacteria | 22 (9.9) |
| *Escherichia coli* | 22 (9.9) |
| *Pseudomonas aeruginosa* | 22 (9.9) |
| Multidrug-resistant *Pseudomonas aeruginosa* | 3 (1.3) |
| *Acinetobacter baumannii* | 3 (1.3) |
| Multidrug-resistant *Acinetobacter baumannii* | 4 (1.8) |
| *Proteus mirabilis* | 13 (5.8) |
| *Proteus vulgaris* | 5 (2.2) |
| *Stenotrophomonas maltophilia* | 4 (1.8) |
| *Serratia marcescens* | 5 (2.2) |
| *Klebsiella pneumoniae* | 8 (3.6) |
| *Morganella morganii* | 4 (1.8) |
| *Citrobacter koseri* | 3 (1.3) |
| Others | 17 (7.6) |
| No growth | 36 (16.1) |

Values are presented as number (%).

gram-positive bacteria among groups (p=0.038; Table 6).

The ratio of wound healing was lowest in group C (7 in wound healing, 23 in amputation) and highest in group D (55 in wound healing, 39 in amputation). There was a statistical significance in difference between the ratio of wound healing of groups (p<0.001; Table 7).

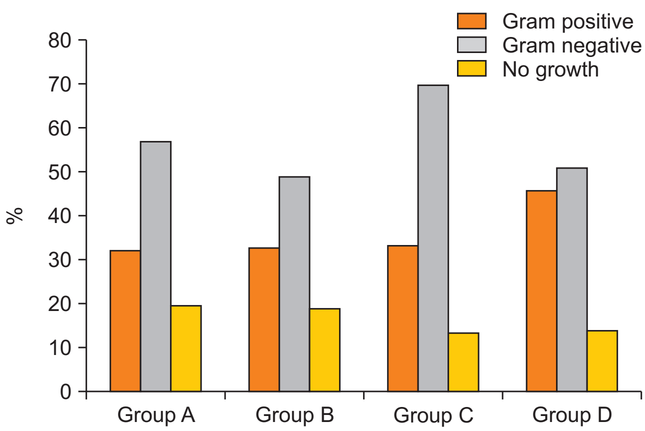


**Figure 1.** This figure demonstrates isolation rate of each comorbidity group. Isolation rate of gram-positive, gram-negative, and non-isolation rate of each comorbidity group (group A~D).

## 4. Correlation of bacterial isolates with wound depth

There were no statistical significance in differences of the isolation rate of gram-positive and gram-negative bacteria and the non-isolation rate of bacteria among grades according to the Wagner classification (Fig. 3). And there were no statistical significance in differences of the isolation rate of MSSA, MRSA, MRGNB, ESBL-producing bacteria and the

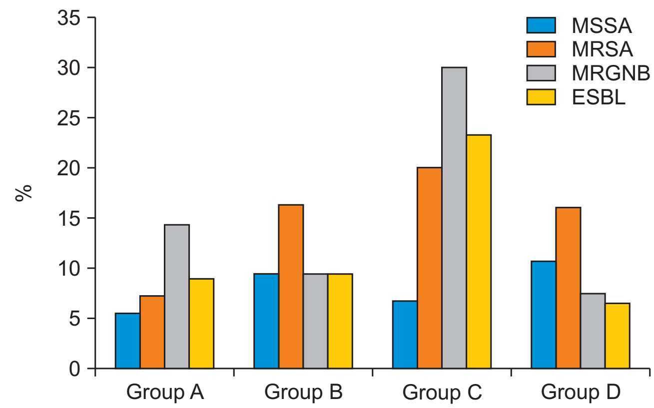


**Figure 2.** This figure demonstrates isolation rate of resistant bacteria of each comorbidity group. Isolation rate of MSSA, MRSA, MRGNB, and ESBL-producing bacteria of each comorbidity group (group A~D). MSSA: methicillin-sensitive *Staphylococcus aureus*, MRSA: methicillin-resistant *Staphylococcus aureus*, MRGNB: multidrug-resistant gram-negative bacteria, ESBL: extended spectrum beta-lactamase.

**Table 5.** Results of Diabetic Foot Ulcer Cultures by Each Disease Group and Chi-Square Analysis

| Variable | Total (n=223) | Group A (n=43) | Group B (n=56) | Group C (n=30) | Group D (n=94) | p-value |
|---|---|---|---|---|---|---|
| Wagner grade | 3.06±1.06 | 3.28±0.94 | 3.18±1.05 | 3.31±1.11 | 2.89±1.11 | |
| Gram-positive | 85 (38.1) | 18 (32.1) | 14 (32.6) | 10 (33.3) | 43 (45.7) | 0.259 |
| Gram-negative | 122 (54.7) | 32 (57.1) | 21 (48.8) | 21 (70.0) | 48 (51.1) | 0.254 |
| No growth | 36 (16.1) | 11 (19.6) | 8 (18.6) | 4 (13.3) | 13 (13.8) | 0.731 |
| MSSA | 19 (8.5) | 3 (5.4) | 4 (9.3) | 2 (6.7) | 10 (10.6) | 0.773 |
| MRSA | 32 (14.3) | 4 (7.1) | 7 (16.3) | 6 (20.0) | 15 (16.0) | 0.284 |
| MRGNB | 28 (12.6) | 8 (14.3) | 4 (9.3) | 9 (30.0) | 7 (7.4) | 0.018* |
| ESBL-producing bacteria | 22 (9.9) | 5 (8.9) | 4 (9.3) | 7 (23.3) | 6 (6.4) | 0.084 |

Values are presented as mean±standard deviation or number (%).
MSSA: methicillin-sensitive *Staphylococcus aureus*, MRSA: methicillin-resistant *Staphylococcus aureus*, MRGNB: multidrug-resistant gram-negative bacteria, ESBL: extended spectrum beta-lactamase.
*Statistically significant (p<0.05).

**Table 6.** Comparative Analysis of Isolation Ratio of Gram-Negative to Gram-Positive of Group A, B, C with Group D

| | Group A (n=43) | Group B (n=56) | Group C (n=30) | Group D (n=94) | p-value |
|---|---|---|---|---|---|
| Gram-positive/gram-negative (n) | 18/32 | 14/21 | 10/21 | 43/48 | 0.038 |

**Table 7.** Comparative Analysis of Ratio of Wound Healing among Groups by Comorbidities

| | Total (n=223) | Group A (n=43) | Group B (n=56) | Group C (n=30) | Group D (n=94) | p-value |
|---|---|---|---|---|---|---|
| Healing/amputation (n) | 90/133 | 11/32 | 17/39 | 7/23 | 55/39 | <0.001 |

**Table 8.** Results of Diabetic Foot Ulcer Cultures by Wagner Classification

| Variable | Grade I (n=13) | Grade II (n=62) | Grade III (n=60) | Grade IV (n=70) | Grade V (n=17) | p-value |
|---|---|---|---|---|---|---|
| Gram-positive | 6 (46.2) | 27 (43.5) | 24 (40.0) | 31 (44.3) | 3 (17.6) | 0.352 |
| Gram-negative | 5 (38.4) | 34 (54.8) | 39 (65.0) | 42 (60.0) | 14 (82.3) | 0.117 |
| No growth | 4 (30.7) | 10 (16.1) | 9 (15.0) | 11 (15.7) | 2 (11.8) | 0.687 |
| MSSA | 3 (23.1) | 10 (16.1) | 5 (8.0) | 1 (1.4) | 0 (0) | 0.064 |
| MRSA | 3 (23.1) | 3 (4.8) | 11 (18.3) | 15 (21.4) | 0 (0) | 0.079 |
| MRGNB | 0 (0) | 8 (12.9) | 8 (13.3) | 10 (14.3) | 2 (11.8) | 0.797 |
| ESBL-producing bacteria | 0 (0) | 7 (11.3) | 5 (8.3) | 9 (12.8) | 1 (5.9) | 0.749 |

Values are presented as number (%).
MSSA: methicillin-sensitive *Staphylococcus aureus*, MRSA: methicillin-resistant *Staphylococcus aureus*, MRGNB: multidrug-resistant gram-negative bacteria, ESBL: extended spectrum beta-lactamase.

**Table 9.** Comparative Analysis of Isolation Rate of Gram-Positive and Gram-Negative Bacteria among Groups by Wagner Classification

| | Grade I (n=13) | Grade II (n=62) | Grade III (n=60) | Grade IV (n=70) | Grade V (n=17) | p-value |
|---|---|---|---|---|---|---|
| Gram-positive/gram-negative (n) | 6/5 | 27/34 | 24/39 | 31/42 | 3/14 | 0.266 |

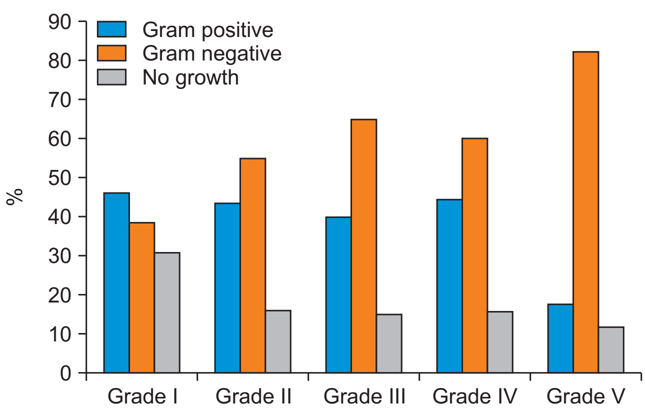


**Figure 3.** This figure demonstrates isolation rate among grades by Wagner classification. Isolation rate of gram-positive, gram-negative, and non-isolation rate of each grade by Wagner classification (grade I~V).

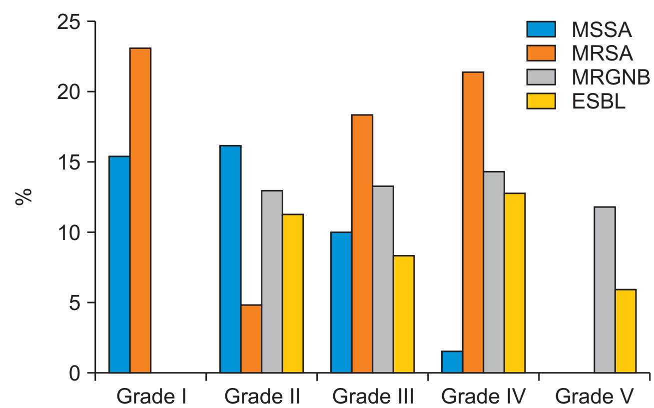


**Figure 4.** This figure demonstrates isolation rate of resistant bacteria among grades by Wagner classification. Isolation rate of MSSA, MRSA, MRGNB, and ESBL-producing bacteria of each grade by Wagner classification (grade I~V). MSSA: methicillin-sensitive *Staphylococcus aureus*, MRSA: methicillin-resistant *Staphylococcus aureus*, MRGNB: multidrug-resistant gram-negative bacteria, ESBL: extended spectrum beta-lactamase.

isolation ratio of gram-negative to gram-positive bacteria among grades (Tables 8, 9, Fig. 4).

## DISCUSSION

The treatment failure of DFU infection at the initial period may lead to lower extremity amputation and sepsis because immunity, in particular, weakens with decreased function of neutrophils. Proper antibiotic treatment appropriate for bacterial isolates identified is the most critical intervention along with surgical debridement and irrigation.[14] Based on the results of bacterial culture and antibiotic susceptibility tests, initial treatment with appropriate antibiotic selection is important. However in clinical practice, it can take several days to get the results of a bacterial culture in primary care clinics. For such a reason as mentioned, the choice of initial antibiotics is usually empirically determined, but inadequate initial antibiotics administration can lead to confoundation for treatment. Therefore we thought it is necessary to develop guidelines for initial antibiotics selections.

The subjects of the present study were 223 patients including 168 (75.3%) male and 55 (24.7%) female with a male-to-female ratio of 3:1. There is almost no difference between male and female in prevalence of diabetes, but male patients were more likely to develop DFU and Benotmane et al.[15] suggested that higher prevalence in male were attributable to lifestyle habits, increased plantar pressure with higher levels of physical activity, and smoking rate.

In other previous domestic studies, isolation rates for gram-positive bacteria were high, ranging between 63.7%~76.4%, while isolation rates for gram-negative bacteria ranged between 33.3%~63.6% in bacterial culture tests for DFU.[16,17] Of all gram-positive bacteria isolated, *S. aureus* was the most commonly detected pathogen at rates of 39.8%~46.3%. *Escherichia coli* was the most commonly found gram-negative bacteria at isolation rates of 13.7%~38.8%. Isolation rates for *P. aeruginosa* ranged between 7.8% and 14.9%.[18] In the current study, the isolation rates of gram-negative bacteria were higher than those of gram-positive bacteria in all groups. The difference in bacterial culture results is thought that patients with more severe ulcer were reviewed in this study because our institution is a tertiary hospital and has a diabetic foot center, so there are many high-risk patients including patients on dialysis for CKD and patients with PAD. In a previous study of Aragón-Sánchez et al.,[19] the isolation rate of higher blood creatine and urea and presence of peripheral artery occlusion could be a predisposing factor to gram-negative diabetic foot osteomyelitis. In this study, there was statistical significance in the isolation ratio of gram-negative to gram-positive bacteria among groups. The difference in the isolation ratio of gram-negative to gram-positive bacteria by group of different comorbidities is anticipated to be resulted from change in immune mechanism and slow tissue recovery mechanism induced by altered tissue osmolarity and decreased peripheral circulation.

This study was limited in certain aspects. First, the control of blood glucose level was not taken into consideration. And type 1 and type 2 diabetes were not differentiated. Second, this study could not consider variability from other underlying diseases such as peripheral neuropathy or weakened immune systems and thoroughly examine a history of antibiotic use before visiting our hospital. Third, patients were analyzed by wound depth according to the Wagner classification and no comparison was done by ulcer size. Fourth, this study is likely to include DFU patients with possibilities of having chronic ulcers or resistant isolates because the subjects were limited to diabetic patients who visited the tertiary hospital. Therefore, selection bias could arise.

The ratio of isolation rate of gram-negative to gram-positive and the isolation rate of multiple resistant bacteria were highest in patients with CKD and PAD. In contrast, there were no significant differences according to wound depth.

## CONCLUSION

This study suggests the use of antibiotics that can cover gram-negative bacteria including MRGNB is considered to lead to better results in the presence of CKD and PAD and initial choice of antibiotics should be considered according to the presence of CKD and PAD rather than wound depth.

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