Incidence and Self-Management of Hand-Foot Syndrome in Patients With Colorectal Cancer

YiYuan Zhao, RN, Yue Ding, RN, YuHan Lu, RN, Jie Zhang, RN, Jin Gu, MD, FACS, and Ming Li, MD, PhD

The purpose of this article is to describe the incidence of hand-foot syndrome (HFS) and self-management of patients with it, including their self-recognition, supportive care, and outcome at home. Study participants were patients with colorectal cancer (CRC) who received adjuvant chemotherapy after surgery. About 67% of participants had HFS, most at grade 1. The majority of patients knew nothing about how to alleviate HFS, and they used no methods to treat it. HFS can worsen the quality of life of patients with CRC receiving adjuvant chemotherapy. The incidence of severe-grade HFS was relatively high in the current study, and patients showed poor self-recognition and self-management. Nurses play a key role in educating patients on how to recognize HFS and use self-management techniques.

With more than 940,000 new cases and about 500,000 related deaths reported worldwide each year, colorectal cancer (CRC) is one of the most common malignancies in the world. In the United States, despite a slight decrease in its incidence and mortality since the 1980s, CRC remains the third most common cancer, with an estimated 102,480 new cases and 50,830 deaths in 2012 (Siegel, Naishadham, & Jemal, 2013).

Combination therapy with surgery is the principle treatment for CRC. XELOX (oxaliplatin plus capecitabine), FOLFOX (oxaliplatin, calcium folinate, and 5-fluorouracil), and capecitabine monotherapy are the most common chemotherapy regimens used for patients with CRC. Those therapies, because of the addition of 5-fluorouracil, capcitabine, and other chemotherapeutics, may cause hand-foot syndrome (HFS) (Janusch et al., 2006).

HFS, also known as palmar-plantar erythrodysesthesia, palmar-plantar erythema, acral erythema, and Burgdorf reaction, is a skin reaction that appears on the palms of the hands or the soles of the feet. The distinctive and relatively frequent toxic reaction is related to certain chemotherapeutic agents. Clinical manifestations of HFS include a prodrome of dysesthesia on the palms and soles, followed in a few days by painful, symmetric, well-defined erythema and edema, which may influence a patient’s quality of life (Gressett, Stanford, & Hardwicke, 2006).

Supportive treatments such as topical wound care, elevation, and cold compresses may help to relieve the pain and could be considered as preventive measures when drugs with a strong association with HFS are going to be administered (Nagore, Insa, & Sanmartin, 2000).

5-fluorouracil and capcitabine, which are important component elements in the CRC chemotherapy regimens of XELOX and FOLFOX, are most frequently associated with HFS. Because most patients are at home between chemotherapy sessions, HFS happens mostly in patients outside of the hospital, so the incidence of HFS and the self-management strategies of patients with CRC to ameliorate the symptoms are seldom reported. Therefore, the authors retrospectively studied 174 patients with CRC who received adjuvant chemotherapy in their institution during a one-year time frame to identify the incidence of HFS.

Methods

Sample

Patients who had histologic or cytologic confirmation of CRC and received adjuvant chemotherapy after surgery from May 1, 2009, to May 1, 2010, in a CRC center in Beijing, China, were enrolled in the study. They had received one of three regimens: XELOX, FOLFOX, or capecitabine alone.
The first cycle of chemotherapy was given six months prior to study participation. A normal mental state was required and patients agreed to be investigated and sign informed consent. Patients who had received chemotherapy before their CRC surgery were excluded. Prior to treatment, all patients were informed about the available treatment options. Chemotherapy with surgery was proposed by doctors to all patients, and each patient had the right to accept or decline. They also were told they had the right to accept or decline study participation and sign an informed consent form. All patients would receive established therapy that was best for them, regardless of study involvement.

**Instrument**

The authors designed a checklist of self-management and had it reviewed by CRC experts. The checklist had seven questions, including topics such as patient self-recognition and supportive self-management care at home. When patients with HFS were identified, the checklist was used to investigate their self-management (see Figure 1).

**Procedure**

With the inpatient database of the authors’ department, potential participants were identified, and all agreed to take part in the interview. Patients were studied retrospectively by telephone after they received one of the three regimens of chemotherapy. All patients were asked the following questions: “Was there any skin reaction during or after your first cycle of chemotherapy?” “What did it look like?” “When did it first happen?” and “How much did it affect your daily life?” The severity of HFS was classified according to the three grades defined by the National Cancer Institute (NCI) (see Table 1). If the patient had HFS, the authors used the checklist to investigate self-management. At the end of the study, all patients and their caregivers were provided with health education about HFS. Patients were told to report HFS to their doctor or nurse if they had any skin reaction after chemotherapy and take pyridoxine to prevent and cure HFS, as research has shown a greater proportion of patients receiving pyridoxine reported symptom improvement compared with those not receiving the agent (65% versus 12%, p < 0.001) (Mortimer et al., 2003). In addition, avoiding impact on their feet (e.g., avoiding tight-fitting socks, excessive exercise) and avoiding hot water (e.g., long showers, hot baths) also were suggested.

**Statistical Analysis**

Descriptive statistics were used to access the incidence and severity of HFS, self-recognition, and self-management of patients. The differences in HFS between the three grades were determined with the Pearson chi-square test. Differences were considered significant when p (two-tailed) was less than 0.05.

**Results**

A total of 174 patients with CRC who received one of three regimens of chemotherapy after surgery were enrolled in the study. Table 2 lists demographic data and disease characteristics for all patients. One hundred and seventeen patients experienced HFS. About 8% of those (n = 9) patients had to undergo drug reduction or withdrawal from their chemotherapy because of HFS (see Table 3), and 27% (n = 31) of patients saw no improvement in their HFS. The median cycle in which HFS first appeared was cycle 2 (range = 1–12 cycles).

The checklist was used to determine the self-recognition and self-management of HFS in these 117 patients. About 28% (n = 33) of patients with HFS received doctor-prescribed treatment to alleviate symptoms of HFS (e.g., dose reduction, drug withdrawal, pyridoxine, emollients). Significantly more treatments were used by those with higher grades of HFS.

**TABLE 1. National Cancer Institute Severity Grades**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Clinical Domain</th>
<th>Functional Domain</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Minimal skin changes of dermatitis (e.g., erythema, peeling) with altered sensations (e.g., numbness, tingling, burning) that do not interfere with activities of daily living</td>
<td>Discomfort insufficient to disrupt normal activities</td>
</tr>
<tr>
<td>2</td>
<td>Skin changes present with accompanying pain interfering little with activities of daily living. Skin surface remains intact.</td>
<td>Discomfort that disrupts activities of daily living</td>
</tr>
<tr>
<td>3</td>
<td>Ulcerative dermatitis or skin changes with severe pain interfering with activities of daily living. Tissue breakdown is evident (e.g., peeling, swelling, blisters, bleeding, edema).</td>
<td>Severe discomfort, unable to work or perform activities of daily living</td>
</tr>
</tbody>
</table>


![FIGURE 1. Checklist of Hand-Foot Syndrome (HFS) Self-Management](image-url)
Discussion

The pathogenesis of HFS has not been determined, but some possible mechanisms have been identified. As a large number of eccrine apparatus lie in the palms and soles, cytotoxic agents tend to accumulate and trigger the immune response in the sweat glands (Innes, 2007). Although HFS is not uncommon, few reports of it exist in the CRC population.

The rates of HFS from chemotherapeutic drugs range from 6%–77% (Gressett et al., 2006; Pendharkar & Goyal, 2004). In the current study, 174 patients with CRC who received the most common adjuvant chemotherapy regimens were retrospectively surveyed. The incidence of HFS was 67%, with 21% experiencing severe (grade 2 or 3) HFS. Those patients experienced severe pain that affected walking, holding things, and general quality of life, and it caused dose reduction or drug withdrawal in about 8% of them.

HFS seems to be dependent on both peak drug concentration and total cumulative dose determination, as the skin reaction tends to be worse if therapy is continued after its development (Nagore et al., 2000). Early recognition, supportive care, and cessation or reduction of drug administration are critical to symptom management (Janusch et al., 2006; Polovich, Whitford, & Olsen, 2007). However, the authors found that although all patients recognized they were experiencing some skin reactions, 17% did not associate it with chemotherapy. Even more remarkable, only 29% (n = 54) of patients reported their skin reactions to medical staff. Nurses should take measures to ensure patients are aware of HFS and promptly report it to the medical staff. Proper assessment and grading are crucial in the assessment of HFS (Viale, 2006).

Nagore et al. (2000) noted that actively preventing and treating HFS (e.g., taking pyridoxol, avoiding hot water) may reduce the incidence and severity of HFS. Prevention and treatment may decrease rates of chemotherapy reduction and withdrawal or even raise tumor remission rates while extending tumor progression stage (Pendharkar & Goyal, 2004). However, the current study indicated that 71% of patients knew nothing about how to alleviate HFS and took no supportive measures to relieve their symptoms. HFS did not get better in 27% of patients because most of the HFS cases first appeared when patients were at home, where they had no resources to consult and used no interventions. In addition, almost 8% had to reduce or stop chemotherapeutic drug regimens because of serious HFS, which may have had an influence on their overall treatment. Oncology nurses are crucial for educating patients about the self-recognition and self-management of HFS (Lassere & Hoff, 2004; Son, Lee, Lee, Yun, & Chun, 2009), so they must offer effective health education before chemotherapy and should monitor patients’ side effects and self-management continuously to guarantee proper treatment. Oncology nurses also have to identify the frequency of occurrence and severity of HFS to determine the most appropriate chemotherapy dose (Janusch et al., 2006). At the end of the current study, all participants were given a list of helpful suggestions to ensure that they reported HFS and carried out self-management at home. Additional follow-up of the incidence and severity of HFS will be conducted in the future.

Supportive care may help to relieve HFS, and it could be of interest to consider these tactics as preventive measures. For example, vitamin B₆ has been used successfully at doses of 100–300 mg per day for treating and preventing fluorouracil-, docetaxel-, etoposide-, and doxorubicin-related palmar-plantar erythrodysesthesia (Nagore et al., 2000). The results of the current study showed that HFS mostly appeared in the early period of chemotherapy, with the median during the second cycle; in some patients, HFS even occurred in the first cycle. Education

### TABLE 2. Patient Demographic and Disease Data (N = 174)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>X</th>
<th>SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>60.26</td>
<td>11.55</td>
<td>31–86</td>
</tr>
</tbody>
</table>

### TABLE 3. Dose Reduction or Drug Withdrawal Caused by Hand-Foot Syndrome (N = 117)

<table>
<thead>
<tr>
<th>Grade</th>
<th>n</th>
<th>Dose Reduction</th>
<th>Drug Withdrawal</th>
<th>%</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0/80</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>2</td>
<td>7/32</td>
<td>4</td>
<td>3</td>
<td>22</td>
<td>–</td>
</tr>
<tr>
<td>3</td>
<td>2/5</td>
<td>–</td>
<td>2</td>
<td>80</td>
<td>–</td>
</tr>
</tbody>
</table>

*Twenty-four patients received more than one regimen.*

FOLFOX—oxaliplatin, calcium folinate, and 5-fluorouracil; HFS—hand-foot syndrome; XELOX—oxaliplatin plus capecitabine
Implications for Practice

- Assessment of hand-foot syndrome (HFS) should be conducted by medical staff prior to every cycle of chemotherapy to maintain quality of life in patients with colorectal cancer.
- Ensure patients report symptoms to medical staff and ask for help as soon as they identify HFS, whether they are in the hospital or at home.
- Patients should be given instructions on identification of HFS, skin care, and protection at the beginning of chemotherapy.

about HFS before chemotherapy is initiated would help ensure continuous chemotherapy and provide a better quality of life for patients during the treatment period.

Conclusion

HFS is a cutaneous skin reaction that appears on the palms of the hands or the soles of the feet that can cause significant discomfort and impairment of function, leading to worsened quality of life in patients with CRC receiving adjuvant chemotherapy. In the current study, patients had a high incidence of HFS that appeared in the early period of chemotherapy. At the same time, patients who experienced HFS had poor recognition and self-management of the syndrome because of insufficient health education. Therefore, effective health education from oncology nurses should be offered to patients with CRC to guarantee identification and self-management of HFS at the very beginning of chemotherapy.

References


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