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Continuous thermographic observation may predict extravasation in chemotherapy-treated patients

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ABSTRACT

Purpose: Extravasation, or leakage of vesicant drugs into subcutaneous tissues, causes serious complications such as induration and necrosis in chemotherapy-treated patients. As macroscopic observation may overlook symptoms during infusion, we focused on skin temperature changes at puncture sites and studied thermographic patterns related to induration or necrosis caused by extravasation.
Methods: Outpatients undergoing chemotherapy using peripheral intravenous catheters were enrolled in this prospective observational study. We filmed and classified infrared thermography movies of puncture sites during infusion; ultrasonography was also utilized at puncture sites to observe the subcutaneous condition. Multiple logistic regression analysis was performed to examine the association of thermographic patterns with induration or necrosis observed on the next chemotherapy day. Differences in patient characteristics, puncture sites, and infusions were analyzed by Mann-Whitney's *U* test and Fisher's exact test according to thermographic patterns.
Results: Eight patients developed induration among 74 observations in 62 patients. Among six thermographic patterns, a fan-shaped lower temperature area gradually spreading from the puncture site (*fan at puncture site*) was significantly associated with induration. Ultrasonography revealed that catheters of patients with *fan at puncture site* remained in the vein at the end of infusion, indicating that the infusion probably leaked from the puncture site. Patients with *fan at puncture site* had no significant differences in characteristics and infusion conditions compared with those with the other five thermographic patterns.
Conclusion: We determined that *fan at puncture site* was related to induration caused by extravasation. Continuous thermographic observation may enable us to predict adverse events of chemotherapy.

1. Introduction

Extravasation is a serious complication in patients with cancer undergoing chemotherapy via peripheral intravenous catheters. Swelling, erythema, and pain are observed as initial symptoms during the infusion. Furthermore, later symptoms, such as induration and necrosis, can be caused by a leakage of vesicant drugs (European Oncology Nursing Society, 2007; Stanford and Hardwicke, 2003). Induration at puncture sites causes difficulty in repeated insertion, and surgical debridement and skin grafting could become necessary for necrosis (Larson, 1982; Wickham et al., 2006). European Oncology Nursing Society suggests careful

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assessment of initial symptoms for the early detection and prevention of severe extravasation (European Oncology Nursing Society, 2007). However, induration and necrosis can occur even if swelling or erythema is not remarkable (de Wit et al., 2013). Furthermore, pain associated with extravasation is difficult to distinguish from venous pain caused by irritation from anticancer agents (Nagai et al., 2013), and patients with neuropathy have difficulty feeling pain (Gonzalez, 2013). Therefore, to evaluate the risk for later extravasation symptoms, a more reliable method is essential other than observation of these initial symptoms during the infusion.

We focused on skin temperature as a novel assessment method for extravasation because cooler skin is considered an extravasation symptom (Hadaway, 2007; Infusion Nurses Society, 2006). An animal experiment showed that leaked agents cooled the subcutaneous tissue, and the temperature of the affected skin surface declined more than that during the correct infusion (Shaeffer et al., 1986). Our group has applied infrared thermography as a useful and noninvasive tool for observing the skin temperature distribution in the clinical setting. We previously reported that the condition of blood flow provided relative temperature changes in pressure ulcer. For example, higher temperature at the wound bed was an inflammatory sign predicting delayed healing (Nakagami et al., 2010), and lower temperature at the wound edge indicated insufficient blood flow developing undermined pressure ulcer (Kanazawa et al., 2016). We now hypothesized that lower temperature of extravasated infusion would affect not only the vein but also the surrounding subcutaneous tissue, and found lower temperature area at puncture sites of patients with infiltration (Oya et al., 2016). It would be a predictor of later extravasation symptoms in chemotherapy-treated patients. Infrared thermography will be a practical device for real-time assessment of the skin temperature distribution during chemotherapy.

It is unknown how the skin temperature distribution changes even during correct chemotherapy infusion. Furthermore, some factors might affect temperature changes in the clinical setting. Therefore, in this study, we first aimed to describe skin temperature changes during chemotherapy using continuous thermographic observation, and investigate a specific thermographic pattern related to extravasation causing induration or necrosis. Second, we evaluated any differences in the characteristics of patients or infusion conditions according to thermographic patterns. We aimed to establish a new prediction method using thermography to identify serious extravasation symptoms in chemotherapy-treated patients.

2. Methods

2.1. Study design and setting

This prospective observational study was conducted in a chemotherapy unit for outpatients in a university hospital in Japan. The number of infusions in this unit is over 5000 a year, including about 75% of infusions through peripheral intravenous catheters and about 20% of infusions using vesicant drugs. Extravasation which needed reinsertion of the catheter occurred in 12 cases (0.23%) in 2015. As the standard of practice in this unit, the size of peripheral intravenous catheter is 24G, infusion pumps are used, and the infusion line is flushed with natural saline in 300 ml/h after administration of anticancer agents. The vein at the forearm is the standard cannulation site, while some patients who do not have the suitable vein for cannulation are catheterized at the wrist and in the antecubital fossa.

The study period spanned February to October 2015. This study was approved by the Research Ethics Committee of the Graduate School of Medicine, The University of Tokyo (#10712). Written informed consent was obtained from all participants.

2.2. Sample

The inclusion criterion was the receipt of chemotherapy through a peripheral intravenous catheter. The exclusion criteria were an age of less than 20 years old and a need to cover the arm during the entire process of chemotherapy, preventing continuous observation of the puncture site by thermography.

2.3. Study measurements

2.3.1. Thermographic observation at puncture sites

We continuously observed the skin temperature distribution at puncture sites during the infusion. An infrared thermography camera was set up using a tripod to permit clear observation of the forearm (approximately 50 cm from the patient). We used a camera that could film a continuous thermal movie (CPA-T420A; FLIR Systems, Inc., Wilsonville, OR, USA). The range, resolution, and accuracy of this camera were −20–120 °C (°C), 0.04 °C, and ±2 °C, respectively. In this study, the frame rate of the camera was set at 1 Hz (Hz), which was enough to observe temperature change during infusion.

The software used to analyze thermographic movies was FLIR Tools Plus (FLIR Systems). The analysis conditions for the software were set as follows. The emissivity value was set at 0.98, and the air temperature was defined as the average of the room temperature at the beginning and end of the infusion. The temperature range was set at 5.0 °C and controlled for each patient to ensure that the maximum temperature at the puncture site did not exceed the range.

2.3.2. Later symptoms of extravasation

Induration or necrosis on the next chemotherapy day was regarded as a later symptom of extravasation. A researcher and clinical nurses, well-experienced with cannulation, including trained chemotherapy nurses observed and palpated the previous puncture site when a patient returned for the next chemotherapy day according to his or her chemotherapy protocol. Induration and necrosis were defined as the site where a catheter could not be reinserted because of the hardness of the skin and the subcutaneous tissue or the need for treatment.

2.3.3. Variables associated with temperature changes

Patient characteristics, puncture sites, and infusions were evaluated as variables associated with temperature changes. Patient characteristics (age, sex, and body mass index) were collected from medical records. The baseline skin temperature before catheter insertion was measured using a skin thermometer (ST-717; Scalar Co., Tokyo, Japan) with an accuracy of ±0.2–0.5 °C. The position of the puncture site (dorsal or ventral side of the arm) was recorded, and the distance from the cubital fossa was measured. To consider the influence of the infusion, the number of cycle of chemotherapy and the maximum drip rate was recorded, and the average of the room temperature before and after the infusion was regarded as the infusion temperature because the infusion bottles were kept in the room temperature for more than 1 h before the administration. The use of a hot compress for preventing vascular pain during the infusion was also recorded.

2.3.4. Ultrasonographic observation

As initial symptoms during the infusion are often unremarkable, we performed ultrasonography at the puncture site before catheter removal to identify extravasation conditions. The subcutaneous