Utility of routine nurse assessment of the risk of chemotherapy-induced febrile neutropenia

by Kelley Moore and Barry Fortner

Abstract

Evidence-based guidelines recommend that patients at high risk (≥20%) for febrile neutropenia (FN) should receive prophylactic colony-stimulating factors (Aapro et al., 2006; Kouroukis et al., 2008; National Comprehensive Cancer Network [NCCN], 2008; Smith et al., 2006). We studied the utility of having nurses routinely assess FN risk in new patients before the initiation of chemotherapy. Fifteen nurses used a standardized tool to evaluate FN risk in 150 patients. In 94% of patients studied, nurses detected risk factors that prompted interventions to reduce the incidence of FN. On final evaluation, 67% of nurses said the use of a standardized tool helped them to identify patients at risk for FN, and 73% planned to assess FN risk routinely. Thus, it is feasible and valuable for nurses to assess FN risk using a standardized checklist prior to the initiation of chemotherapy.

Chemotherapy-induced neutropenia and its consequences are a constant concern of oncology nurses. Febrile neutropenia (FN) is estimated to affect at least 25% to 40% of treatment-naive patients receiving common chemotherapy regimens (Dale, 2002). About a third of patients with FN develop a microbiologically confirmed infection (Cordonnier et al., 2005; Gayán-Martinez et al., 2005) and, in Canada, there are approximately 7,000 hospitalizations for neutropenia each year (Desjardins & Meuller, 2005). Although most patients requiring hospitalization have successful outcomes, mortality during FN-associated hospitalization is 7% to 10% (Caggiano, Weiss, Rickert, & Linde-Zwirble, 2005; Kuderer, Dale, Crawford, Cosler, & Lyman, 2006). Febrile neutropenia also often results in dose reductions and/or delays during treatment of early stage breast cancer (Lyman, Dale, & Crawford, 2003) or non-Hodgkin's lymphoma (Lyman, Dale, Friedberg, Crawford, & Fisher, 2004). There is increasing evidence that dose modification lessens the potential for long-term disease control and reduces survival in patients who have potentially curative malignancies (Bonadonna, Valagussa, Moliterni, Zambetti, & Brambilla, 1995; Budman et al., 1998; Epelbaum et al., 1990; Kwak, Halpern, Olshen, & Horning, 1990; Lyman, 2005).

A randomized, controlled phase III trial has demonstrated that primary prophylaxis with granulocyte colony-stimulating factor (G-CSF) significantly reduces the incidence of FN, as well as FN-related hospitalizations and IV antibiotic use, when given with a moderately myelosuppressive chemotherapy regimen (Vogel et al., 2005). In response to these findings, three sets of guidelines for CSF use have been published or updated by different American and international organizations (Aapro et al., 2006; National Comprehensive Cancer Network [NCCN], 2008; Smith et al., 2006). In addition, Canadian recommendations for the use of supportive care in the management of neutropenia have also been published (Kouroukis et al., 2008). The international consensus according to these guidelines is that the risk of FN should be assessed prior to the first cycle of chemotherapy. Furthermore, these guidelines also state that prophylactic CSF should be given if the chemotherapy regimen is associated with an FN risk ≥20%, or if the chemotherapy-related risk of FN is 10% to 20% and certain patient-related risk factors are present. Support with a CSF is also recommended to reduce the need for dose reductions or delays during adjuvant therapy, curative therapy, or therapy intended to prolong survival. The guidelines of the European Organisation for Research and Treatment of Cancer (EORTC) provide an algorithm for risk assessment and decision-making about prophylactic G-CSF use (Figure 1). Numerous examples of regimens with a risk of FN ≥10% are also listed in the EORTC guidelines.

Oncology nurses are the primary advocates for supportive care for patients, and they can be instrumental in identifying patients at high risk for FN. However, the baseline results of the AIM Higher Initiative, a quality improvement program that is collected data until 2008, suggest that many nurses do not routinely assess a patient’s risk of neutropenia (Johnson, Moore, & Fortner, 2007). This initiative is designed to optimize supportive care by improving cancer-related symptom assessment, patient education, and management for five chemotherapy-related symptom groups: anemia, neutropenia, diarrhea and constipation, nausea and vomiting, and depression and anxiety. Of the 376 adult cancer patients who were surveyed as part of the AIM Higher Initiative at 15 community oncology clinics in the United States, only 96 (26%) had documented evidence of pre-treatment risk assessment for neutropenia.

There has been substantial evidence from nurse-led studies that the identification of patients at high risk for FN, followed by G-CSF prophylaxis, when indicated, could improve patient outcomes such as reducing dose delays and dose reductions and avoiding FN-related hospitalizations (Lenhart, 2004; Donohue, 2006; Doyle, 2006; White, Maxwell, Michelson, & Bedell, 2005). We conducted a study to test our hypothesis that a standardized process of FN risk assessment would help nurses be proactive in reducing the risk of...
chemotherapy-induced neutropenia. Secondary goals of the study were to document nurses' perceptions of how a risk assessment tool could be useful to them and to identify which patient care interventions were common after risk assessment.

**Methods**

This exploratory study was entitled “Feasibility of Utilizing the Amgen Chemotherapy-Induced Neutropenia Risk Assessment Tool in Clinical Oncology.” It was conducted at the 15 community oncology practices that were participating in the AIM Higher Initiative, although this project was a separate undertaking from the initiative. With the assistance of the nurse champion at each AIM Higher site, the nurse participants for this study were identified. Between July and December 2004, 15 nurses at 15 independent practices used a checklist to evaluate the risk of FN in the next 10 adult chemotherapy patients (total of 150 patients) that they encountered for new patient assessment and teaching; each patient need not have been chemotherapy-naïve, but was starting a new chemotherapy regimen. Patients did not have to meet any additional eligibility criteria. We did not use informed consent in this study, because we were evaluating the nurses’ experience with using the new patient assessment tool. No personal patient information was provided to the investigators. In addition, the assessment tool remained with the patients’ charts; only the nurses’ evaluations of the tool were provided to the investigators.

We used a checklist made available by Amgen Inc. (Figure 2); this tool was complete and incorporated the most recent data available at the time of the study's start. The same tool has also been used in other quality improvement studies, such as the one conducted by Doyle (2006). Using this particular checklist, patients with one or more risk factors were identified as being at risk for FN and as candidates for prophylactic growth factor support.

After performing the risk assessment, nurses recorded the patient risk factors identified and the interventions initiated in response to their findings. After each patient encounter, they also completed a written questionnaire that was developed by the investigators in which they rated the extent to which the routine use of a risk assessment tool was helpful with regard to patient care (Figure 3). The questions were specifically designed to address the objectives of the study, namely (i) to determine the utility of the chemotherapy-induced neutropenia (CIN) risk-assessment tool in the clinical oncology setting, (ii) to evaluate nurses’ perceptions of how the tool can facilitate proactive management of CIN, and (iii) to highlight the most common patient risk factors and actions taken in response to the findings in the risk assessment. For each question, multiple possible answers were provided. Nurses were asked to rank their agreement with the answer on a scale of 1 to 5 with 1 being strongly disagree and 5 being strongly agree.

After each nurse had used the risk assessment tool on the tenth and last patient and had completed the corresponding questionnaire, the nurse also completed a final survey, which was developed by the investigators to address the overall usefulness of incorporating a risk assessment tool into normal clinical practice (Figure 4, page 78). Specifically, nurses were asked if they would incorporate into their practice the CIN risk-assessment checklist used in this study or another similar tool. As in the other questionnaires, nurses were asked to rank their agreement with the answer on a scale of 1 to 5.

Descriptive statistics were used to analyze the data providing results by site and for the total sample. Frequency tables were generated for categorical variables. Variance indicators, including standard deviation and confidence intervals, were calculated for continuous variables.

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**Patient Evaluation for Chemotherapy-Induced Neutropenia Management**

<table>
<thead>
<tr>
<th>Patient Name</th>
<th>Date</th>
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**Chemotherapy Risk Factor**

- Chemotherapy regimen associated with a moderate to high risk of neutropenic complications

**Independent Risk Factors**

- Age > 70 years
- Preexisting neutropenia
- Extensive prior chemotherapy
- Previous irradiation to marrow sites
- History of recurrent FN while receiving previous chemotherapy
- Poor performance status
- Advanced cancer
- Decreased immune function, e.g., diabetes, COPD
- Open wounds
- Active tissue infection
- Serum albumin ≤ 3.5 g/dL (NHL)
- Elevated serum LDH (NHL)
- Bone marrow involvement
- Patients undergoing dose-intense therapy

**Patient’s Need for Growth Factor Support**

- Patient is a candidate for growth factor support.
  - Schedule an injection appointment.
  - Provide a prescription for growth factor.
  - Repeat growth factor with subsequent cycles of this regimen.
- Patient is not a candidate for growth factor at this time; monitor closely.

Physician signature: Date:

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**Figure 1.** European Organisation for Research and Treatment of Cancer algorithm for decision-making about use of prophylactic granulocyte colony-stimulating factor (G-CSF). FN = febrile neutropenia. Source: Aapro et al., 2006. Reprinted from *European Journal of Cancer*, 42, 2433–2453. Copyright 2006, with permission from Elsevier.

**Figure 2.** Evidence-based standardized tool used in this study to assess patients at high risk for febrile neutropenia (FN). COPD = chronic obstructive pulmonary disease; LDH = lactate dehydrogenase; NHL = non-Hodgkin’s lymphoma.
Results

All 15 nurses who participated in the study were already routinely involved in assessing, interviewing, and educating new patients (Table 1). On average, they had 12 years of oncology experience. Of the 150 patients, 110 (73%) were female, and breast cancer and gynecologic cancers constituted nearly half of the primary cancer sites.

In the questionnaires they completed immediately after conducting each of the 10 risk assessments, nurses indicated that using a standardized tool helped them to assess the risk of FN in 72% of patients and to determine the degree of FN risk in 57% (Figure 5). The majority of the patients (83 patients, 55%) were eligible for G-CSF prophylaxis because they were scheduled to receive a moderately to highly myelosuppressive chemotherapy regimen. In addition, substantial proportions of patients had characteristics that warranted consideration of G-CSF prophylaxis. The most commonly identified of these patient-related risk factors for FN were advanced cancer (46 patients, 31%), age > 70 years (33 patients, 22%), impaired immune function (19 patients, 13%), and extensive prior chemotherapy (18 patients, 12%).

For the vast majority of patients (141 patients, 94%), findings noted during the risk assessment prompted one or more interventions to lessen the duration of severe chemotherapy-induced neutropenia and its complications, such as FN and infection. The intervention relied on most frequently, in 96 patients (64%), was closer monitoring of the patient for FN. Other interventions were the prescription of prophylactic G-CSF (41 patients, 27%), a change in the choice of chemotherapy regimen (three patients, 2%), and a change in the dose of chemotherapy (one patient, 0.7%). The fifth option on the questionnaire, changing the schedule of chemotherapy, was not reported by any of the nurses.

On final assessment, almost all the nurses, 13 of 15 (87%), said they had found it easy to use a risk assessment tool. In addition, 67% said using a tool helped them determine which patients were at risk for FN, and 73% said their practice planned to assess FN risk routinely in the future using the same tool or a similar method. The two nurses who were unlikely to use the same or similar tool in the future expressed the concern that this checklist evaluated patients for only one symptom, namely neutropenia. Because nurses routinely assess patients for multiple symptoms and adverse effects, they suggested that a single tool that could assess patients for multiple symptoms would have greater utility.

Discussion and conclusions

The results of this nurse-initiated study indicate that prior to initiation of chemotherapy, it is feasible and valuable for oncology nurses to assess adult patients’ risk of FN. In nearly all of the 150 patients they assessed (94%), nurses detected risk factors that prompted them to take action to reduce the incidence of severe chemotherapy-induced neutropenia and its complications.

A standardized risk assessment tool such as the one used in this study is applicable across a wide range of tumour types. It can be readily incorporated into routine practice, judging from the fact that 87% of nurses in this study rated it easy to use. Risk information is not always present in a patient’s chart before treatment, and a checklist provides a framework for nurses to ask additional questions during the patient interview. The use of a standardized tool should also make it easier to maintain consistent quality of patient assessment throughout the practice.

### Neutropenia Risk Assessment

<table>
<thead>
<tr>
<th>Neutropenia Risk Assessment</th>
</tr>
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<tbody>
<tr>
<td>Date of assessment: 2027-05-31</td>
</tr>
<tr>
<td>Age: 52 years</td>
</tr>
<tr>
<td>Gender: Female</td>
</tr>
<tr>
<td>Marital status: Married</td>
</tr>
<tr>
<td>Employment status: Full-time</td>
</tr>
<tr>
<td>Education level: College</td>
</tr>
<tr>
<td>How far do you live from the hospital? 10 miles</td>
</tr>
<tr>
<td>How long does it take to get to the hospital? 10 minutes</td>
</tr>
<tr>
<td>Cancer diagnosis: Breast</td>
</tr>
<tr>
<td>Stage: II</td>
</tr>
<tr>
<td>Chemotherapy regimen: Docetaxel 75 mg/m² on Day 1, every 21 days</td>
</tr>
<tr>
<td>Comments:</td>
</tr>
</tbody>
</table>

Figure 3. Questionnaire evaluating the extent to which the routine use of a risk assessment tool was helpful to nurses. Reproduced with permission from Supportive Oncology Services.
The consensus from the guidelines and recommendations of different organizations from the U.S., Europe and Canada is that risk assessments should be performed routinely before the first cycle of chemotherapy. (Aapro et al., 2006; Kouroukis et al., 2008; NCCN, 2008; Smith et al., 2006). Each of the three guidelines, however, offers slightly different guidance about which risk factors for chemotherapy-induced FN should be evaluated. Oncology nurses should focus on adapting these national and international evidence-based guidelines to develop practice-specific risk assessment tools that are relevant to their own practice environment and patient populations (Maxwell & Stein, 2006). For example, Donohue identified risk factors for neutropenia based on published guidelines and literature and extracted a simplified list of factors that were applicable to all non-leukemia cancer patients (Donohue, 2006). Regardless of the specific tool that is used, it should be included in the patient chart for sharing information with other providers.

As new evidence becomes available and risk assessment tools continue to be refined, it will become possible to more definitively identify patients who require G-CSF prophylaxis and/or require additional nursing interventions to prevent or manage FN (Lyman, Lyman, & Agboola, 2005). New knowledge about risk factors became available even during the course of our study, which led to changes in the consensus guidelines. For example, at the time that our study was initiated, patients over 70 years were defined in the NCCN guidelines as being associated with greater FN risk. More recent guidelines have identified patients 65 years or older as having greater risk for FN (Aapro et al., 2006; Smith et al., 2006; NCCN, 2008). The use of a standardized tool that is frequently revised to reflect the most recent evidence makes it less likely that newly identified risk factors will be overlooked.

A number of nurse-initiated studies (Donohue, 2006; Doyle, 2006; Lenhart, 2004; White et al., 2005) have shown that systematic identification of patients at high risk for FN, followed by G-CSF prophylaxis, as necessary, can improve patient outcomes with regard to neutropenic events. Improvements have included significant reduction in the need for chemotherapy dose delays (Donohue, 2006) and significant reductions in the rate of FN-related hospitalization and the length of hospital stay (Doyle, 2006). The current study builds on the previous work in confirming that routine prechemotherapy assessment prompts nurses and other health care professionals to take action that can minimize their patients’ risk of FN.

Nurses often face barriers to implementing a new tool, especially lack of time and lack of acceptance from coworkers. It is important to adopt an easy-to-use tool, basing it on an existing questionnaire or

### Table 1. Nurse and patient characteristics

<table>
<thead>
<tr>
<th></th>
<th>Nurses (N = 15)</th>
<th>Patients (N = 150)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y, mean (SD)</td>
<td>39.0 (10.8)</td>
<td>58.3 (12.7)</td>
</tr>
<tr>
<td>Oncology experience, y, mean (SD)</td>
<td>12.0 (9.0)</td>
<td></td>
</tr>
<tr>
<td>Involved in assessing and interviewing new patients, %</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>Involved in educating new patients, %</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>Primary cancer site, no. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breast</td>
<td>50 (33.3)</td>
<td></td>
</tr>
<tr>
<td>Gynecologic</td>
<td>24 (16.0)</td>
<td></td>
</tr>
<tr>
<td>Lung</td>
<td>21 (14.0)</td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>18 (12.0)</td>
<td></td>
</tr>
<tr>
<td>Non-Hodgkin’s lymphoma</td>
<td>11 (7.3)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>26 (17.4)</td>
<td></td>
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<tr>
<td>Primary cancer stage, no. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>22 (14.7)</td>
<td>41 (27.3)</td>
</tr>
<tr>
<td>II</td>
<td>41 (27.3)</td>
<td>35 (23.3)</td>
</tr>
<tr>
<td>III</td>
<td>30 (20.0)</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>22 (14.7)</td>
<td></td>
</tr>
</tbody>
</table>

Figure 4. Final survey evaluating the overall usefulness of incorporating a risk assessment tool into normal clinical practice. Reproduced with permission from Supportive Oncology Services.

Figure 5. Nurses’ perceptions of the usefulness of a febrile neutropenia risk assessment tool. G-CSF = granulocyte colony-stimulating factor.
evidence-based algorithm (see Figure 1), and to explain to clinic physicians and other staff that use of the tool can translate into improved care and increased efficiency. Maxwell and Stein (2006) present detailed suggestions for nurses who wish to integrate guidelines for FN assessment into clinical practice, including a sample checklist, a sample algorithm for determining which patients need CSF support, and a list of strategies for overcoming barriers.

It is also important to solicit feedback from team members in an effort to address the needs of the staff. For example, in our study, a few nurses suggested that a single tool that could assess patients for multiple symptoms would be more useful than a tool that evaluated only one potential adverse effect, namely neutropenia. Based on this feedback, the nurse champions from the AIM Higher Initiative developed a multi-symptom risk-assessment tool. (Johnson et al., 2007). Integrating multisymptom risk assessments into electronic medical records may be another strategy that could help overcome this barrier.

Nurses are the members of multidisciplinary patient-care teams who are best positioned to assess patients' risk of FN. Using a simple and practical tool, nurses can potentially have a substantial positive impact on neutropenic events in patients who are undergoing myelosuppressive chemotherapy.

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References


