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Evidence-Based Cancer Imaging

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With the advances in the field of oncology, imaging is increasingly used in the follow-up of cancer patients, leading to concerns about over-utilization. Therefore, it has become imperative to make imaging more evidence-based, efficient, cost-effective and equitable. This review explores the strategies and tools to make diagnostic imaging more evidence-based, mainly in the context of follow-up of cancer patients.

Keywords: *Evidence-based imaging; Cancer imaging; Computerized physician order entry; Clinical decision support*

INTRODUCTION

Imaging has assumed a central role in the care of cancer patients, from the initial diagnosis to metastatic surveillance and treatment monitoring. With the advent of molecular targeted therapy and immune checkpoint inhibitors, several treatment options are available to treat majority of the malignancies. For example, nine novel molecular targeted agents and immune checkpoint inhibitor have received US Food and Drug Administration -approval for treatment of advanced renal cell carcinoma (RCC) in the last decade. As a result of these advances in management, cancer patients are living longer, and frequently undergo prolonged imaging follow-up to assess for metastatic disease. This increasing use of imaging has led to concerns about over-utilization, escalating costs, radiation burden and potential patient anxiety (1-3). Therefore, it has become imperative to make imaging more evidence-based, efficient, cost-effective and equitable in order to maintain, and even further increase, its value in clinical care. The 2001 Institute of Medicine's report on healthcare quality "Crossing the Quality Chasm" advocates a care system consisting of high performing patient-centered approach, with the aim of achieving safe, effective, efficient, personalized, timely and equitable care (4). The proposed principles to redesign the health system to provide high quality care include, among others, evidence-based decisions, reducing the waste, and personalized care. Although these strategies were not specific to radiology, they are certainly applicable to imaging. This review explores the strategies to make diagnostic imaging more evidence-based, efficient, reliable and cost effective, mainly in the context of follow-up of cancer patients. Advances are also being made in the field of image-guided minimally-invasive therapy; however, this review will not include the evidence-based interventional imaging strategies.

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Evidence-Based Cancer Imaging: Needs and Challenges

Over the last three decades, the field of human genomics has rapidly advanced, sparking an exponential interest and discoveries in the other "-omic" fields, including radiogenomics. These advances, accompanied by developments in targeted therapies, have brought 'precision oncology', to the forefront of cancer treatment. For example, patients with non-small cell lung cancer with activating somatic mutation of the epidermal growth factor receptor respond well to tyrosine kinase inhibitors gefitinib and erlotinib (5), while patients with anaplastic lymphoma kinase (ALK) rearrangement dramatically benefit from an ALK receptor tyrosine kinase inhibitor crizotinib (6). Knowledge of the von Hippel-Lindau-hypoxia-induced factor pathway leading to vascular endothelial growth factor (VEGF) and platelet-derived growth factor driven angiogenesis has allowed successful use of VEGF-targeted therapies in patients with clear cell RCC (7).

While there is an increasing trend towards personalizing cancer treatment, the field of evidence-based imaging has not advanced as rapidly. There is still marked variability in the use of imaging for oncologic patients which can be attributed to referring physicians' personal preferences, lack of evidence-based data, and in part because of patient expectations and inability of both patients and physicians to accept uncertainly regarding diagnosis (8). Decisions regarding the use of imaging are often based on individual clinician experience, and in some cases, on consensus guidelines (9, 10). There is a need to generate additional robust evidence-based recommendations so that imaging utilization can be optimized for cancer patients. Another challenge in forming evidence-based guidelines for oncologic patients is the rapid evolution of genomics and cancer treatments, resulting in changing trends in clinical practice. Therefore, there is a need for ongoing evidence development and resultant adaptation of imaging practices (11).

Incidental Findings and Evidence-Based Imaging

Incidental findings are commonly encountered in routine clinical practice, in both oncologic and non-oncologic settings. The exact frequency of incidental findings remains unknown; however, Furtado et al. (12) reported that 86% (1030/1192) patients undergoing whole-body screening CT of the chest, abdomen and pelvis had at least one abnormal finding and 37% (445/1192) of these received at least one recommendation for further evaluation. Low-radiation dose unenhanced CT performed for CT colonography has been reported to show clinically significant incidental findings in 5–16% of patients (1). In a large study including nearly 6 million diagnostic imaging examination reports, the rate of recommendation for additional imaging increased from 6% to 12% from 1995 to 2008 (13). While the majority of incidental findings are benign and do not need any further intervention, their detection often leads to additional testing that increases costs, patient anxiety and radiation dose (2). At present, the optimum imaging work-up protocol of these lesions also remains unknown (1) because there is no robust evidence-base to guide the management of incidental findings. In such a situation, we must resort to the next best option which is consensus-based guidelines. In 2010, the first white paper of the American College of Radiology (ACR) Incidental Findings Committee on management of incidental findings on abdominal CT was published (1), followed by additional papers focusing on specific organs (14-17).

Incidental adnexal lesions are a specific example of this phenomenon. Such lesions are common, reportedly found in 2.5–18% of postmenopausal women (18-20). The risk of malignancy in these lesions is low; yet the majority undergo further imaging evaluation because of fear of an underlying malignancy (18-20). Therefore it is important to have guidance on the optimum evaluation strategy of these lesions. The ACR white paper on adnexal findings provides guidance on management of incidental adnexal lesions based on the imaging features on CT (or MRI), size and menopausal status of the patient (14). These consensus guidelines are based on, and complement, guidelines by the Society of Radiologists in Ultrasound for ultrasound (21). However, studies have shown that a significant proportion of patients with incidental adnexal lesions undergo work-up that is not adherent to the guidelines. In a study by Kim et al. (22) the current guidelines were not followed in 50% of patients, perhaps because of barriers to adherence such as lack of awareness, previous practice habits, lack of local practice "buy-in", shortage of time and difficulty in incorporating the guidelines in practice (23). The same group demonstrated that local adaptation of the existing guidelines and incorporating them into a radiology decision support tool significantly improved the rate of guideline-adherent evaluation of incidental adnexal lesions (22). A similar approach is possible with incidental findings in the other organs.

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Metastatic Surveillance and Evidence-Based Imaging

At present, surveillance and follow-up of oncologic patients in the United States is guided by the National Comprehensive Cancer Network (NCCN) clinical practice guidelines (10). The majority of the NCCN recommendations are consensus-driven, based on lower-level strength of evidence (10, 24). Despite the guidelines, there is marked variability in the use of imaging for these patients. It is important to personalize and optimize the follow-up imaging strategy in oncologic patients because novel anticancer agents have improved their outcomes and these patients are frequently followed with imaging for a longer duration. As we gain insights into the cancer biology and individual risk factors affecting outcomes, it is critical to incorporate these into the imaging decision process.

We can explore this concept further with the example of ovarian cancer. Ovarian cancer is the fifth most common cause of cancer mortality in women, responsible for an estimated 22280 new cases and 14240 deaths in 2016 in the United States alone (25). The majority of the patients with ovarian cancer present with advanced (stage III and IV) disease (26, 27). The overall 5-year survival of advanced ovarian cancer ranges between 19–47% (28). Because of relatively long survival, these patients undergo imaging follow-up over a prolonged duration, usually with CT. Despite a relatively low incidence of thoracic metastases in these patients, chest CT is commonly used to follow these patients; currently there is limited evidence-based guidance for the use of cross-sectional chest imaging in the follow-up of these patients (29-31). Optimization of imaging evaluation of these patients would be beneficial in order to reduce costs and more effectively utilize available resources. The radiation dose associated with chest CT may also be an important consideration in these patients because of radiation to the breasts (32, 33).

We have recently shown that thoracic metastases in patients with ovarian cancer typically develop late in the disease course and almost always occur with preexisting or prior abdominal disease (34). Moreover, the presence of disease on abdominal imaging was the only factor independently associated with thoracic metastases, and the initial thoracoabdominal metastases were almost always visible on abdominal imaging (34). Therefore, it seems that there is an opportunity to reduce the utilization of chest CT in patients with ovarian cancer with a consequent reduction in the associated costs and radiation dose, especially to the breast tissue (32, 33).

Similar approaches can be used with other malignancies to optimize the follow-up imaging protocols. In patients with gastrointestinal stromal tumor (GIST), we have previously shown that limiting the cross-sectional chest imaging to patients who have bulky abdominal metastases could substantially reduce the use of chest CT, with minimal risk of missing thoracic metastasis (35). Joensuu et al. (36, 37) have shown, also in patients with GIST, that imaging may be more efficiently used if the frequency of imaging follow-up is tailored to the risk of recurrence. These reports by our group and by Joensuu et al. (36, 37) complement each other in forming the right imaging strategy for patients with GIST. Similar work is needed in the other malignancies to form evidence-based strategies to scan the appropriate body segment at an appropriate interval.

Use of Technology to Choose the Right Test

Several technological tools are currently available to extract evidence and incorporate evidence-based imaging strategies in routine clinical practice.

Computerized Physician Order Entry with Embedded Clinical Decision Support

Over the last decade, computerized physician order entry (CPOE) has become an integral part of patient management. CPOE also opens the door for use of advanced information technology (IT) tools including clinical decision support (CDS), and offers an opportunity to reduce waste and improve the quality of care (38). Besides improved workflow, adoption of CPOE along with embedded CDS, has also shown positive effects on physician imaging ordering practices, including a decline in the proportion of low utility examinations ordered (39-41).

Clinical decision support involves presentation and display of contextualized, brief and actionable information to providers at appropriate times to enhance clinical decisions at point of care. CDS helps providers determine the necessity for imaging and assists in choosing the optimal diagnostic study. CDS consists of an evidence-base and its logical clinical recommendation, and a computer program that delivers the evidence to the user based on the discrete data entered by the user into the computer (42). The evidence-base may consist of local best practices or existing professional society guidelines such as ACR appropriateness criteria® or NCCN clinical practice guidelines (10, 43). CDS can be in the form of alerts, pop-up prompts, customized order sets for specific clinical situations, templates, information buttons, or links to knowledge base. CDS in the context of imaging promotes evidence-based decisions, reduces inappropriate imaging, reduces waste and improves quality (38). In order to be effective, CDS should target a well-defined knowledge gap, should be based on a current and diverse evidence-base, should receive multidisciplinary input and buy-in, the strength of the underlying evidence should be transparent to the users, and it should provide brief, unambiguous and actionable recommendations with minimal disruption to clinical workflow (42). Establishing a feedback mechanism or specific consequences for ignoring the CDS enhances the impact of CDS as an educational tool (44). At our institution, several CDS-enabled interventions have been successfully implemented over the past decade (41, 44, 45), and a vast potential for oncologic applications exists. Experience at our and other institutions has shown that implementation of CDS leads to an improvement in the quality of care and adherence to guidelines (22, 41, 44, 45).

Natural Language Processing

With millions of imaging studies being performed every year, it is almost impossible to manually review all the reports and/or medical records in order to extract the data to develop an additional evidence-base for patients with cancer. Natural language processing (NLP) is a field of computational linguistics that deals with the interactions between computer and human (natural) languages. NLP has found a useful role in medical informatics and evidence-based medicine because it allows batch processing of a large number of medical documents, including radiology reports and clinic notes, to extract context-specific information (46). Investigators have used NLP to screen radiology reports to study the rates of recommendations for additional imaging (13). NLP has been used to identify the rate and contributing factors of repeat abdominal imaging studies (47). We have also used NLP to identify patients with GIST in order to develop a decision rule to help optimize the use of chest CT in these patients (35).

Structured Reports

Radiology report serves as an official record of the imaging procedure and its results. 2007 ACR Intersociety Conference concluded that radiology report is a key area for imaging practice improvement (48). It is expected that wider use of structured reports would standardize the quality of the reports and reduce unwarranted variation, and help in better communication of the imaging findings to the referring physicians, leading to improved clinician satisfaction (48-51). Structured reports can also help the radiologists as an effective educational tool leading to quality improvement (52). The Radiological Society of North America has developed a library of reporting templates pooled from various sources including different institutions and radiology societies, in order to identify and promote the best practices in reporting (53). At our institution, implementation of a structured report for rectal cancer staging led to improvement in the quality of MRI reports (54). With the wider use of electronic health records (EHR), once these structured reports get integrated into the EHR, this wealth of standardized information would become available to the radiologists for research, data mining and to understand the trends in imaging utilization (48).

Critical Results Notification System

Closed-loop communication of critical or unexpected results from diagnostic procedures among caregivers, mainly from the radiologist to the referring physician, is an important patient safety issue (55). Communicating and documenting important findings detected on imaging studies helps ensure the appropriate management of critical findings and adequate follow-up of incidentally detected potentially important findings, such as an incidental pulmonary nodule or an enhancing renal lesion. Traditionally, this communication and documentation has relied on labor-intensive processes. At our institution, we have implemented an electronic system called Alert Notification of Critical Results (ANCR) to facilitate communication of critical findings. ANCR is integrated into the radiologist's workflow and automatically populates the fields such as patient name, medical record number, details of the imaging study; it can be used to communicate the results via email or pager, and also serves as closed-loop documentation of the communication, thus also serving as a source of data for relevant regulatory and safety audits (56).

CONCLUSION

The increasing importance of imaging in the management of oncologic patients comes with challenges related to both under- and overutilization. Imaging needs to keep pace

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with precision oncology by developing optimized evidence-based imaging strategies. Evidence-based guidelines are necessary for evaluation of incidental findings as well as for the follow-up of oncologic patients. CPOE, CDS, NLP tools and critical results notification systems are some of the available tools which can help optimize imaging for care of oncologic patients.

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