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Streamlining the Imaging of Clinically Suspected Pheochromocytoma: Using Urine Metanephrines to Decrease Imaging Costs

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Abstract

Purpose: To improve the cost efficiency of the imaging evaluation of clinically suspected pheochromocytoma by using 24-hour fractionated urine metanephrine (FUM) results.

Methods: A retrospective review of I-123 meta-iodo-benzyl-guanidine single photon emission tomography (SPECT) computed tomography (CT) studies performed at our institution between January 2007 and February 2011 for clinically suspected pheochromocytoma was performed. SPECT-CT results from 70 patients were compared with results from 24-hour FUM analysis (within 2 months of SPECT-CT) and with relevant CT or magnetic resonance imaging studies (within 6 months of SPECT-CT). An imaging algorithm was developed to maximize cost efficiency without altering the final imaging interpretation. Actual imaging costs for the studied cohort were compared with the expected costs if this algorithm had been applied.

Results: If the 24-hour FUMs were normal, then all the SPECT-CT studies were negative (16/70). Eighty-seven percent of patients with abnormal total metanephrine had a positive SPECT-CT. If the total metanephrine was normal but 1 or more of the metanephrine fractions were abnormal, then 39%-58% of the SPECT-CT studies were positive. Within this subgroup, none had a positive SPECT-CT if a CT or magnetic resonance image was negative or benign. The actual imaging costs averaged CAD$2833.19 per patient for this cohort. Applying a streamlined imaging algorithm guided by 24-hour FUM analysis would result in an average imaging cost of CAD$1225.97 per patient without an expected change in the final imaging impression.

Conclusion: By using 24-hour FUM results to streamline imaging, considerable cost savings per patient (56.7%) can be attained without a change in the final overall imaging interpretation.

Résumé

Objectif: Améliorer le rapport-efficacité des évaluations d'imagerie des phéochromocytomes présumés en utilisant les résultats des métanéphrines urinaires fractionnées (MUF) sur 24 heures.

Méthodologie: On a effectué un examen rétrospectif de gammatomographies réalisées avec de la méta-iodo-benzyl-guanidine radiomarquée à l'iode 123 dans notre établissement de janvier 2007 à février 2011 dans des cas de phéochromocytome présumé sur le plan clinique. Les résultats des gammatomographies de 70 patients ont fait l'objet d'une comparaison avec les résultats d'une analyse des MUF sur 24 heures (dans les 2 mois suivant la gammatomographie) de même qu'avec les résultats de TDM et d'examens d'imagerie par résonance magnétique pertinents (dans les 6 mois suivant la gammatomographie). Un algorithme d'imagerie a été mis au point pour maximiser le rapport coût-efficacité sans altérer l'interprétation finale des examens d'imagerie. Les coûts réels des examens d'imagerie subis par la cohorte étudiée étaient comparables aux coûts attendus si cet algorithme avait été appliqué.

Résultats: Lorsque les MUF sur 24 heures étaient considérées comme normales, alors l'ensemble des gammatomographies se révélaient négatives (16/70). Quatre-vingt-sept pour cent des patients affichant des métanéphrines totales normales ont présenté des résultats positifs à la gammatomographie. Lorsque les métanéphrines totales étaient normales, mais qu'une ou plusieurs métanéphrines fractionnées étaient considérées comme anormales, alors 39 à 58 % des gammatomographies étaient positives. Au sein de ce sous-groupe, aucun patient n'a présenté une gammatomographie positive lorsqu'une TDM ou qu'un examen d'imagerie par résonance magnétique était négatif ou bénin. Pour cette cohorte, les coûts réels moyens d'imagerie étaient équivalents à 2833,19 $ CA par patient. L'utilisation d'un algorithme d'imagerie simplifiée guidée par l'analyse des MUF sur 24 heures entraînerait des coûts d'imagerie moyens de 1225,97 $ CA par patient, sans altération prévue de l'impression d'imagerie finale.

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Conclusion: En utilisant les résultats des MUF sur 24 heures en vue de simplifier l'imagerie, des économies considérables par patient (56,7 %) peuvent être réalisées sans modifier l'interprétation d'imagerie globale et finale.

Key Words: Pheochromocytoma; Single photon emission tomography computed tomography; I-123/I-131 meta-iodo-benzyl-guanidine; Metanephrines

Pheochromocytomas (intra-adrenal paragangliomas) are rare neuroendocrine neoplasms that arise from chromaffin cells of the adrenal medulla [1]. The prevalence of pheochromocytoma is estimated to be approximately 0.1%-0.6% of patients with hypertension [2], with an annual incidence of approximately 2-8 per million persons per year [3]. Pheochromocytomas produce catecholamines, including epinephrine, norepinephrine, and/or dopamine, which are then metabolized primarily intratumourally to form metanephrines [4]. The clinical symptomatology that results from the production of catecholamines and/or metanephrines is nonspecific and variable. The classic clinical triad includes headaches, excessive sweating, and palpitations and/or tachycardia; however, this only occurs in 10%-36% of patients [5,6]. Other symptoms include paroxysmal or sustained hypertension, fatigue, weight loss, hyperglycemia, pallor, and nausea. Pheochromocytomas should be considered in patients with classic symptomatology, discovery of a suspicious incidental adrenal mass or in a patient with familial disease. The majority of diagnosed cases are sporadic; however, at least 25% of cases may be associated with familial diseases such as von Hippel-Lindau disease, multiple endocrine neoplasia type 2, neurofibromatosis type 1, or succinate dehydrogenase mutation [7].

For clinically suspected pheochromocytomas, the first diagnostic examination performed is typically a biochemical assessment for excess catecholamines or metanephrines. Commonly, these include 24-hour fractionated urine metanephrines (FUM) (with or without vanillylmandelic acid), total plasma metanephrines (metanephrine and normetanephrine), and plasma concentration of free metanephrines. The decision of which biochemical test to use is debated and variable among institutions, and a general consensus has not been established [8−10]. FUMs typically measure the 24-hour urinary excretion of metanephrine (metabolite of epinephrine), normetanephrine (metabolite of norepinephrine), 3-methoxytyramine (metabolite of dopamine), and the total concentration of metanephrines. The sensitivity of FUMs is high and ranges from 90%-97%, with a specificity that ranges from 69%-98% [8−10]. Generally, biochemical tests for pheochromocytomas have a high negative predictive value, of approximately 95%-100% [11]. Given the low incidence and prevalence of pheochromocytoma, the positive predictive value is generally low and difficult to accurately determine given varying pretest probabilities [10]. This leads to a high rate of false-positive results, which necessitates the need for additional tests. After a positive biochemical analysis, an imaging examination is often performed to improve specificity.

Several imaging methods are available for further evaluation of clinically suspected pheochromocytoma, including anatomic imaging modalities such as computed tomography (CT) and magnetic resonance imaging (MRI) as well as functional imaging modalities such as I-123/I-131 meta-iodo-benzyl-guanidine (MIBG) [12−15]. Given the highly variable appearance of pheochromocytomas, anatomic imaging modalities have high sensitivities but lower specificities. When compared with anatomic imaging, functional imaging is generally more specific (95%-100%); however, its sensitivity is more limited (77%-90%) [16,17]. Additional strengths of functional whole-body imaging methods include assessment of extra-adrenal pheochromocytomas, metastatic disease, and/or tumour recurrence.

With the recent introduction of hybridized single photon emission tomography CT (SPECT-CT) technology, anatomic and functional imaging modalities are combined maximizing sensitivity and specificity [18−20]. As such, this imaging method has become a common imaging technique used in patients suspected of having a pheochromocytoma after a positive biochemical analysis; however, an exact association between the quantitative biochemical parameters and imaging findings has not been established. Given the low positive-predictive value of elevated urine metanephrines and the relatively high cost of I-123 MIBG SPECT-CT, it is likely not cost efficient to perform this imaging study on every patient with this biochemical abnormality. In clinical practice, these patients also are often imaged in a nonlinear fashion (ie, ''shotgun approach'') and receive multiple imaging tests, including CT, MRI, and/or SPECT-CT, which further increases imaging costs. When considering this, the goal of our study was to develop a cost-efficient approach to imaging clinically suspected pheochromocytoma by using the FUM results to streamline our approach.

Materials and Methods

Study Design and Study Population

A retrospective chart review of all patients who had an I-123 MIBG SPECT-CT study between January 2007 and February 2011 was performed. The protocol was reviewed and approved by our institutional research ethics board. All SPECT-CTs were supervised and interpreted by trained licensed specialists in nuclear medicine in accordance with standard clinical practice. Based on a review of the imaging reports, the results were recorded as positive, negative, or nondiagnostic for pheochromocytoma. The 24-hour FUM results that were closest to the date of the SPECT-CT (within