The prevalence of hydronephrosis on renal ultrasound in patients with acute kidney injury : a systematic review and meta-analysis

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Introduction

Acute kidney injury (AKI) is defined as an acute, sustained decline in both the filtration and excretory function of the kidney, leading to a buildup of toxic waste products in the blood, seen clinically as azotemia, or an increase in serum creatinine values. AKI is a common clinical condition among hospitalized patients, affecting 5-7% of all hospitalized patients, and up to 23% of those in the intensive care unit (ICU) (Huang, Lee, Chen, Chuang, & Chen, 2005). It is associated with increased morbidity and mortality, length of stay, and overall cost of care (Chertow, Burdick, Honour, Bonventre, & Bates, 2005; Liangos et al., 2006). Renal ultrasound is frequently performed on patients presenting with AKI in order to rule out hydronephrosis, a dilatation of the renal collecting system from the buildup of urine, as a sign of obstruction, one of the most common and easily treatable causes of the condition. The appropriate use of ultrasound in this setting, however, continues to be debated (Faubel, Patel, Lockhart, & Cadnapaphornchai, 2014).

AKI has a wide range of etiologies that can be divided into three distinct categories: prerenal, intrinsic, and postrenal/ obstructive (Barozzi, Valentino, Santoro, Mancini, & Pavlica, 2007). Early determination of the cause, especially in urinary tract obstruction, is an important step in restoring function to the kidney and reducing morbidity and mortality. To make this determination, practitioners utilize a combination of methods: collection of a thorough medical history, frequent blood chemical measurements, urine microscopy, and medical imaging (Podoll, Walther, & Finkel, 2013).

The American College of Radiology Appropriateness Criteria®, a set of evidence-based guidelines that rank imaging procedures according to their ability to assess a given clinical condition, rates renal ultrasound as most appropriate for evaluation of AKI. This recommendation is based on its ability to “assess renal size and echogenicity” and to “exclude bilateral obstruction in high-risk groups” (Remer et al., 2014). Ultrasound is also portable and readily available, making it especially beneficial in intensive care units (ICU), where some of the highest percentages of patients are affected (Huang et al., 2005). In addition, renal ultrasound is non-invasive, relatively inexpensive, and does not impart a radiation risk to the patient (Gamss et al., 2015). Clinicians, therefore, often order renal ultrasound to exclude obstructive causes of AKI before moving to more invasive tests for further investigation. Recent studies, however, have found that ultrasound evaluation is only clinically useful in patients whose medical history directly points to increased risk of obstructive pathology.

The purpose of this systematic review and meta-analysis is to combine data from multiple studies that have researched the prevalence of hydronephrosis in patients undergoing renal ultrasound for evaluation of acute kidney injury, in order to determine the clinical utility of ordering this scan, both in the general population, and in the lower risk population.

Materials and Methods

Literature Review

A comprehensive data search was performed in order to find all relevant articles relating to renal ultrasound in the setting of acute kidney injury. One researcher performed the search, and assistance was provided by Jolene Miller, MLS, a librarian and the director of the Mulford Health Science Library at the University of Toledo. The search engines used were PubMed, Embase, and Web of Science.

The search entry used for PubMed was: (((obstruction OR hydronephrosis OR azotemia OR "serum creatinine")) AND acute kidney injury [Mesh]) AND ultrasonography [Mesh] This search yielded 113 articles, of which 93 were available in English.

The search entry used for Embase was: ('ultrasound'/exp OR ultrasound OR 'ultrasonography'/exp OR ultrasonography AND (acute AND ('kidney'/exp OR kidney) AND ('injury'/exp OR injury) OR acute AND renal AND failure OR 'azotemia'/exp OR azotemia OR 'serum creatinine'/exp OR 'serum creatinine') AND ('obstruction'/exp OR obstruction OR 'hydronephrosis'/exp OR hydronephrosis) AND (prevalence OR 'clinical utility' OR 'diagnostic value')). This search yielded 71 results, of which five articles overlapped with the PubMed search. However, no additional articles were determined to be relevant to the research question.

The search entry used for Wed of Science was: TS(topic)= ((ultrasound OR ultrasonography) AND (acute kidney injury OR acute renal failure OR azotemia OR “serum creatinine”) AND (obstruction OR hydronephrosis) AND prevalence). This search yielded 8 results, of which none were found to be unique, relevant articles compared to the first search.

In addition to these two searches, a manual search was performed in which the references of all relevant articles were scanned. Google Scholar was also utilized. This manual search revealed one additional unique article that was deemed to be relevant to the research question, for a total of 114 articles.

Criteria for Inclusion and Exclusion

Articles were individually evaluated for their relevance to the research question. For an article to be included, it had to be a primary article presenting original research on adult patients with AKI who underwent renal ultrasound testing. Articles needed to have calculated the total number of patients who underwent testing, as well as the number and/or percentage of those patients whose ultrasound revealed hydronephrosis of one or both kidneys.

Articles were excluded from this systematic review and meta-analysis for the following reasons: 1) Subject matter not relevant to the research question (e.g. patients were not evaluated using renal ultrasound); 2) Article not available in the English language. There were no exclusion criteria established for date of publication, as detection of hydronephrosis should not be affected by advances in ultrasound scanning technology. After the inclusion and exclusion criteria were applied, a total of nine articles were determined to be suitable for analysis.

Data Extraction

The following data was extracted from the nine articles: first author, year of publication, country where the study was conducted, study design, number of patients who underwent renal ultrasound for the diagnosis of acute kidney injury, and number of patients in whom hydronephrosis was detected via ultrasound. Prevalence of hydronephrosis was either extracted directly as reported, or calculated using the published tables and figures. For articles in which patients were further stratified into high and low risk groups for the presence of hydronephrosis, the following additional data was extracted: The number of low risk patients who underwent renal ultrasound evaluation, the number of low risk patients in whom hydronephrosis was subsequently found, and the criteria by which “low risk” was established.

Outcomes of Interest

The goal of this systematic review and meta-analysis is to demonstrate that only a small percentage of renal ultrasounds ordered for acute kidney injury subsequently find renal obstruction as the cause of injury. The variable analyzed in the meta-analysis will be the mean prevalence of hydronephrosis on renal ultrasound performed for the evaluation of acute kidney injury. Additionally, the mean prevalence of hydronephrosis in low risk patients will be separately analyzed using those studies that reported this data.

Statistical Analysis

Data was analyzed using the Review Manager software version 5.3 developed by Cochrane ("Review Manager (RevMan)," 2014). The random-effects model was used to determine average prevalence of hydronephrosis on renal ultrasound across studies. The tests were performed with 95 percent confidence intervals. In order to determine heterogeneity between the studies, Forest plots for each set of data were created and chi-squared values were analyzed, in which a statistically significant value represents evidence of heterogeneity. According to Cochrane, however, chi-squared tests have low power in analyses in which studies have low sample sizes or are few in number. Therefore, I^2 values were also interpreted according to *The Cochrane Handbook* guidelines, using the following overlapping thresholds: 0 to 40% might not be important, 30 to 60% may represent moderate heterogeneity, 50 to 90% may represent substantial heterogeneity, and 75 to 100% represents considerable heterogeneity. (*Cochrane Handbook for Systematic Reviews of Interventions* 2011).

Funnel plots to detect publication bias were also created for each data set. The funnel plots are scatter plots in which the measured prevalence for each study was plotted against the standard error, as calculated by $SQRT\ (p * \frac{1-p}{n})$, where *p* is prevalence and *n* is the total sample size, or the number of patients included in analysis.

Results

Selection of Studies

Of the 114 articles that were collected via the formalized search, 21 were eliminated because they were not available in the English language. The remaining 93 articles were reviewed using the title and abstract to determine their relevance to the research question. After the exclusion criteria were applied, a total of nine unique articles remained.

Of the nine articles deemed appropriate for analysis, seven were retrospective chart reviews and two were prospective studies. All studies were conducted in the United States, except Huang et al., which was conducted in Taiwan. Two studies, Keyserling et al. and Huang et al. focused solely on patients in the Intensive Care Unit. Overall, 2930 patients who underwent renal ultrasound for the evaluation of acute kidney injury were investigated (Table 1).

The studies by Keyserling et al. and Stuck et al. were unique to the others in that their exclusion criteria for patients were more restricting, so that essentially only low risk patients were included in their analysis. These low risk patients in Keyserling et al.'s study included those who had no history of obstructive uropathy or nephrolithiasis, abdominal or pelvic mass, BPH, or recent blunt abdominal trauma (Keyserling, Fielding, & Mittelstaedt, 2002). Patients in Stuck et al.'s study included those without known renal mass, obstructive uropathy or nephrolithiasis, or symptoms such as flank mass, flank pain, or hematuria (Stuck, White, Granke, Ellis, & Weissfeld, 1987).

In addition to these studies, articles by Ritchie et al., Licurse et al., Gamss et al., and Ip et al. further stratified their results into high and low risk groups, so that prevalence among low risk groups was also calculated (Gamss et al., 2015; Ip, 2016; Licurse et al., 2010; Ritchie, 1988). Criteria for low risk group inclusion can be found in Table 2.

Average Prevalence Analysis

All nine studies were included in the analysis of average prevalence of hydronephrosis on renal ultrasound for patients with AKI. A total of 3727 patients with AKI were evaluated using renal ultrasound. Of those, 332 were found to have hydronephrosis. The average prevalence of hydronephrosis among the studies was calculated at 0.08, or 8% (95% CI= 0.05 to 0.12). The chi-squared value of 169.54 ($P<0.00001$), and I^2 value of 95% both show considerable heterogeneity among the studies. The high degree of heterogeneity is possibly due to the difference in methodology among the various studies. For example, two studies excluded patients that were deemed high risk from their data, thereby increasing their risk of bias compared to the other studies. In addition, the studies' patient populations varied. For example, Keyserling et al. and Huang et al. focused their studies only on patients in the Intensive Care Unit, and Huang et al. took place in Taiwan (Huang et al., 2005; Keyserling et al., 2002). Figures 1 and 2 represent a summary of this analysis.

Six studies further stratified their results to separate patients who were at a decreased risk for hydronephrosis, and therefore those six studies were included in a separate analysis to calculate average prevalence of hydronephrosis on renal ultrasound in low risk patients with AKI. The total number of low risk patients scanned with renal ultrasound was 1169. Of those low risk patients, only 25 were subsequently found to have hydronephrosis. The average prevalence of hydronephrosis on low risk patients was calculated to be 0.02, or 2% (95% CI= 0.01 to 0.03). The chi-squared value of this analysis was 7.32, with a p value of 0.12, which is not statistically significant for heterogeneity. Analysis of the more accurate I^2 value of 45% may represent moderate heterogeneity among the included studies. This lower heterogeneity is likely due to the fact that these five studies used similar methods to determine low risk populations, therefore decreasing methodological diversity. Figures 3 and 4 represent a summary of this analysis.

Discussion

AKI is defined as an acute, sustained decline in both the filtration and excretory function of the kidney, leading to a buildup of toxic waste products, such as urea, in the blood. It occurs in a wide variety of settings, with a range of clinical manifestations. Because of this, no widely accepted standard for diagnosis currently exists. Most clinicians, however, make the determination based on a rise in serum creatinine, which is usually associated with a concurrent decline in urine output (Barozzi et al., 2007). An initiative by Bagga et al. classified the severity of the injury into three stages based on these two values. For example, a rise of serum creatinine of 0.3 mg/dl with a urine output of less than 0.5 ml/kg per hour would place a patient in stage 1 AKI, the least severe of the stages. The authors, however, recognize that further research is necessary in order to validate the criteria (Bagga et al., 2007). In addition, serum creatinine is not an exact indicator of renal function, as it can be decreased in elderly patients with a reduced muscle mass (Gamss et al., 2015).

AKI has a variety of etiologies. Hypoperfusion, a prerenal cause of injury, can be due to stenosis of the renal arteries, low cardiac output, or decreased fluid volume, as in dehydration. The most common intrinsic cause, as well as the most frequently seen overall, is acute tubular necrosis (ATN). Research into the pathophysiology of ATN has found that several mechanisms are involved: direct cell injury, intrarenal vasoconstriction, destruction by reactive oxygen species, and activation of inflammatory pathways (Barozzi et al., 2007). Other intrinsic causes of AKI include interstitial, glomerular, and small vessel disease. Postrenal causes are least commonly seen, and are related to bilateral urinary tract obstruction, leading to a backup of urine into the kidney’s collecting system. Obstruction and the resulting hydronephrosis can be caused by bilateral (or unilateral in the case of a solitary kidney or with pre-existing low-functioning kidney) urethral stones, retroperitoneal fibrosis, or infiltration of the ureters by malignancy from any of the pelvic organs (Remer et al., 2014).

Postrenal causes of AKI, though rare, are often the most easily reversed. In a study by Gamss et al., for example, the serum creatinine levels improved in 82% of patients that received some form of treatment after hydronephrosis was discovered (Gamss et al., 2015). For this reason, it is important for clinicians to quickly identify patients with a possible obstruction and to begin the proper treatment. Renal ultrasound is a quick and cost effective method of making this diagnosis. It has been shown to identify the hydronephrosis caused by obstruction with a high degree of sensitivity (Faubel et al., 2014).

Renal ultrasound is not without its risks, however. Although the presence of hydronephrosis on ultrasound imaging is assumed to be due to obstruction, and the lack of hydronephrosis ruling out obstruction, both false negatives and false positives do exist. Hydronephrosis may not be evident during early stages of obstruction or in patients who are dehydrated (Gamss et al., 2015). For example, a case report by Spital et al. presents four patients with severe renal failure secondary to obstruction. Of these four patients, minimal dilatation was seen via imaging in only one, yet relief of obstruction led to renal function improvement in all four (Spital, 1988).

Hydronephrosis can be seen without the presence of obstruction in chronic reflux disease, rapid diuresis, and pregnancy (Gamss et al., 2015). Therefore, even when hydronephrosis is seen, additional imaging, including diuretic renography or Doppler imaging for ureteral jets, may occasionally be needed to confirm the presence of true obstruction (Faubel et al., 2014). In addition, renal ultrasound may demonstrate incidental findings that are not related to the patient’s current condition. A study of 104 patients by Keyserling et al. included incidental findings of 16 simple cysts, 4 nonobstructing renal calculi, 2 duplicated collecting systems, and 2 solid renal masses. Some of these findings likely led to additional, and in some cases unnecessary, testing in order to further define the pathology (Keyserling et al., 2002). For these reasons, it is important to study the conditions in which renal ultrasound is currently ordered for AKI, and to determine the clinical utility of doing so in all patients.

To date, there has not been a meta-analysis performed that combined all available data on the prevalence of hydronephrosis on renal ultrasound. Our meta-analysis was performed to determine the average prevalence among the available studies, and to further evaluate prevalence once only low risk patients were included, so that clinicians might have increased knowledge when deciding whether or not to order renal ultrasound testing. Our meta-analysis calculated that an average of 8% (95% CI= 5% to 12%) of patients who underwent renal ultrasound for AKI were subsequently found to have hydronephrosis suggesting obstruction. When the analysis was narrowed to focus only on those patients considered to be low risk for obstruction based on past medical history, the average prevalence decreased to only 2% (95% CI= 1% to 3%). We can therefore conclude that the diagnostic yield of renal ultrasound to rule out obstruction as the cause of a patient's AKI, especially when those at high risk based on history are excluded, is low. These results suggest that for those patients at low risk for obstruction, the benefits of performing such a study may not outweigh the potential risks of increased cost and potential further imaging to classify incidental findings. In this setting, it may be beneficial to the patient to postpone or completely eliminate the need for renal ultrasound imaging.

The funnel plots for each of our analyses show a publication bias. According to Cochrane, when the results of smaller studies with fewer participants (and therefore higher standard error) remain unpublished, the funnel plots will show a gap in one of the bottom corners, as is seen in both Figures 2 and 4. When this occurs, the result of the meta-analysis is often over-estimated (*Cochrane Handbook for Systematic Reviews of Interventions* 2011). As a result of all included studies in our analyses having relatively similar sample sizes, it is possible that in real-world settings, the prevalence may be even lower than those calculated.

Our meta-analysis has several strengths. First, it is the first such systematic review and meta-analysis on the topic of prevalence of hydronephrosis in acute kidney injury. Second, our analysis included both retrospective and prospective research, which adds strength to the overall study. Finally, the data included was collected from a variety of medical centers and departments, including several large teaching hospitals across the United States, Intensive Care Units, and one hospital in Taiwan.

Our meta-analysis has several limitations. The first is the number of included studies. Nine studies including a total of 3727 patients were analyzed, however more studies would have added additional information and strength to the analysis. Additionally, only six of the included articles furthered stratified patients into high and low risk groups, so only these patients could be included in prevalence analysis in the low risk population. A second limitation is that in the low risk analysis, the six studies used different criteria in order to determine low risk, so these studies cannot be directly compared. A third limitation is that the protocols for performing the ultrasound examinations, nor for the radiologist's determination of hydronephrosis when reading the exams were not studied. Differences in these protocols cannot be excluded, and would potentially affect the outcomes. Furthermore, this meta-analysis did not include analysis on the sensitivity, specificity, or positive predictive value of renal ultrasound in detecting hydronephrosis or in establishing hydronephrosis as the definite cause of the patients' acute kidney injury. Some patients included in this analysis may have had hydronephrosis on ultrasound that was later determined not to be clinically relevant and thus would alter the data. Further testing and analysis would be required to determine the relevance of this information.

Conclusion

Although renal ultrasound is frequently ordered to evaluate patients who develop acute kidney injury, hydronephrosis as the cause of the condition is infrequently seen, especially in those considered low risk based on past medical history. The data from this original systematic review and meta-analysis supports the idea that renal ultrasound, which is not without cost and possible risk to the patient, should not be ordered on patients with AKI, unless history and co-morbidities strongly point to obstruction.

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Table 1: Characteristics of included studies

Study	***Year***	***Country***	***Study Design***	***Total no. of pts***	***No. of pts with hydronephrosis***	***Percentage***
Stuck et al.	1987	USA	Prospective	189	7	3.70
Ritchie et al.	1988	USA	Retrospective chart review	394	38	9.64
Gottlieb et al.	1996	USA	Retrospective chart review	60	21	35.00
Keyserling et al.	2001	USA	Retrospective chart review	105	1	0.95
Huang et al.	2004	Taiwan	Retrospective chart review	320	5	1.56
Licurse et al.	2010	USA	Retrospective cross-sectional	797	84	10.6
Podoll et al.	2013	USA	Retrospective cohort	810	42	5.19
Gamss et al.	2014	USA	Retrospective chart review	274	28	10.22
Ip et al.	2016	USA	Prospective, observational cohort	778	106	13.62

Table 2: Criteria for low risk

Study	***Criteria for low risk***
Stuck et al.	NO known obstructive uropathy, calculi, renal mass, hematuria, flank mass, flank pain
Ritchie et al.	NO known pelvic malignancy, palpable abdominal or pelvic mass, suspected renal colic, known renal calculous disease, bladder outlet obstruction, recent (<1 mo) pelvic surgery, suspected urinary sepsis
Keyserling et al.	NO history of obstructive uropathy or nephrolithiasis, clinically diagnosed abdominopelvic masses, BPH, recent major blunt abdominopelvic trauma
Licurse et al.	NO previous history of hydronephrosis AND less than 2 points from the following: recurrent UTIs (1 point), diagnosis consistent with possible obstruction (1 point), nonblack race (1 point), absence of exposure to inpatient nephrotoxic medications (1 point), absence of congestive heart failure (1 point), absence of prerenal AKI (1 point)
Gamss et al.	NO pelvic mass (including BPH), prior renal or pelvic surgery, histroy of neurogenic bladder
Ip et al.	Licurse model (see above)

Study or Subgroup	Prevalence	SE	Weight	Prevalence IV, Random, 95% CI	Year
Stuck et al.	0.037	0.01	12.0%	0.04 [0.02, 0.06]	1987
Ritchie et al.	0.096	0.01	12.0%	0.10 [0.08, 0.12]	1988
Gottlieb et al.	0.35	0.06	5.2%	0.35 [0.23, 0.47]	1996
Keyserling et al.	0.01	0.01	12.0%	0.01 [-0.01, 0.03]	2001
Huang et al.	0.016	0.01	12.0%	0.02 [-0.00, 0.04]	2004
Licurse et al.	0.11	0.01	12.0%	0.11 [0.09, 0.13]	2010
Podoll et al.	0.052	0.01	12.0%	0.05 [0.03, 0.07]	2013
Gamss et al.	0.102	0.02	10.8%	0.10 [0.06, 0.14]	2014
Ip et al.	0.136	0.01	12.0%	0.14 [0.12, 0.16]	2016
Total (95% CI)			**100.0%**	**0.08 [0.05, 0.12]**	

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 169.54$, df = 8 ($P < 0.00001$); $I^2 = 95\%$
Test for overall effect: $Z = 4.70$ ($P < 0.00001$)

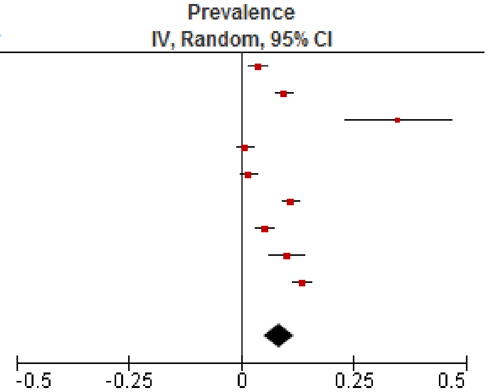

Figure 1: Forest plot for average prevalence of hydronephrosis on renal ultrasound

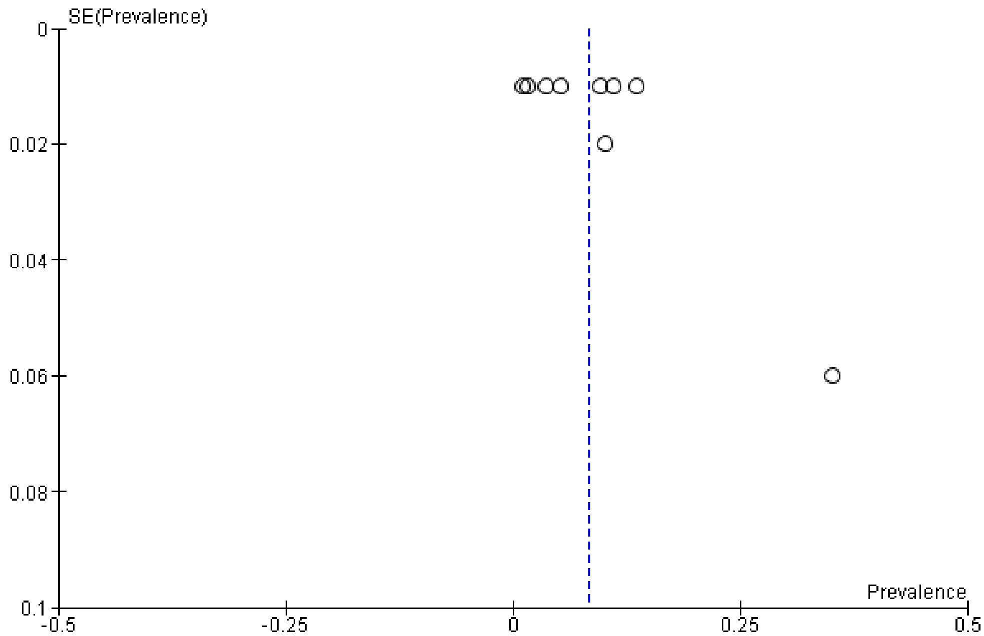

Figure 2: Funnel plot for average prevalence of hydronephrosis on renal ultrasound

Study or Subgroup	Prevalence	SE	Weight	Prevalence IV, Random, 95% CI	Year
Stuck et al.	0.037	0.014	14.0%	0.04 [0.01, 0.06]	1987
Ritchie et al.	0.011	0.006	32.4%	0.01 [-0.00, 0.02]	1988
Keyserling et al.	0.01	0.009	23.7%	0.01 [-0.01, 0.03]	2001
Licurse et al.	0.031	0.012	17.2%	0.03 [0.01, 0.05]	2010
Gamss et al.	0	0		Not estimable	2014
Ip et al.	0.04	0.015	12.7%	0.04 [0.01, 0.07]	2016
Total (95% CI)			**100.0%**	**0.02 [0.01, 0.03]**	

Heterogeneity: Tau² = 0.00; Chi² = 7.32, df = 4 (P = 0.12); I² = 45%
Test for overall effect: Z = 3.43 (P = 0.0006)

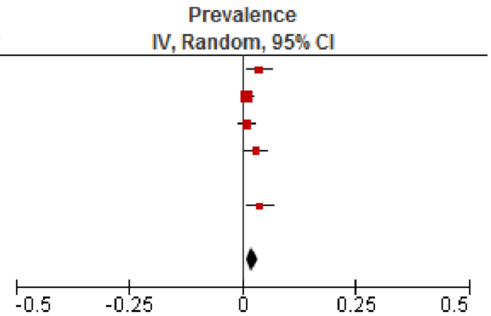

*Figure 3:*Forest plot for average prevalence of hydronephrosis in low risk patients on renal ultrasound

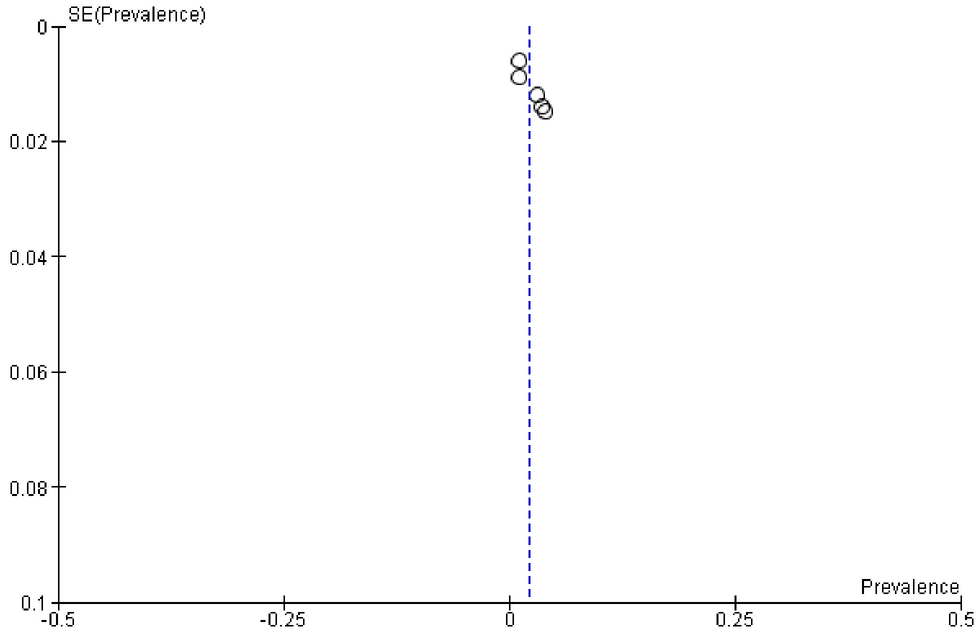

Figure 4: Funnel plot for average prevalence of hydronephrosis in low risk patients on renal ultrasound

Abstract

Objective: We aimed to combine data from all studies that determined the average prevalence of hydronephrosis seen in patients undergoing renal ultrasound in the setting of acute kidney injury (AKI), in order to determine the clinical utility of ordering this scan, both in the general and low-risk patient populations. **Methods**: We conducted a systematic review and meta-analysis of all studies that determined the prevalence of hydronephrosis found on renal ultrasound performed in the setting of AKI. A second meta-analysis was conducted using only those studies which determined prevalence of hydronephrosis in low risk patients. **Results**: The average prevalence of hydronephrosis among all patients with AKI was 0.08, or 8% (95% CI= 0.05 to 0.12). The average prevalence of hydronephrosis on low risk patients was 0.02, or 2% (95% CI= 0.01 to 0.03). **Conclusion**: In patients with AKI who lack high-risk criteria for hydronephrosis, renal ultrasound is probably not indicated.