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Meta-analysis of the Effect of Automated Contrast Injection Devices versus Manual Injection and Contrast Volume on Risk of Contrast Induced Nephropathy

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Abstract

Contrast sparing devices have been slowly adopted into routine patient care. Randomized trial evidence of automated contrast injectors (ACIs) has not been analyzed to evaluate the true reduction in contrast volume during coronary angiography and intervention. It is thought that by reducing the amount of contrast exposure there will be a simultaneous reduction in the risk of CIN. Therefore, we sought to synthesize published evidence on contrast sparing devices, contrast volume and incidence of contrast-induced nephropathy (CIN). We searched Medline, The Cochrane Library, and ClinicalTrials.gov. Search criteria included ACIs compared to manual injection, contrast media volume and incidence of CIN. Data was extracted by two independent reviewers. Weighted mean difference of contrast volume was calculated using random effects models in RevMan 5.4.1 software to derive a summary estimate. A total of 79,694 patients from 10 studies were included (ACI arm n= 20,099; Manual injection arm n= 59,595). On average, ACIs reduced contrast volume delivery by 45 mL per case ($p < 0.001$, 95%CI: -54, -35). CIN incidence was significantly reduced by 15% with an odds ratio of 0.85 ($p<0.001$, 95%CI: 0.78, 0.93) for those utilizing ACIs compared to manual injection. In conclusion, ACIs in angiography significantly reduces the volume of contrast delivered to the patient and the incidence of CIN.

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Keywords

automated contrast injectors; contrast volume; contrast induced nephropathy

Introduction

To date, several studies have compared manual injection to ACIs and have reported a reduction in contrast volume administered with use of ACIs.(1-7) Studies have varied in the reported reduction of contrast for diagnostic catheterization.(1-4, 6-9) Others also include the contrast volume utilized during percutaneous coronary intervention (PCI).(1-5, 7, 9) However, there is a significant gap in summarizing the evidence in the published literature. With several studies reporting varying results in the utilization of ACIs compared to manual injection a meta-analysis or systematic review of the current research is required. The sample size of several of the studies is small and the combined power of a meta-analysis may allow for a more powerful conclusion based on the evidence. Therefore, we conducted a meta-analysis examining the currently published evidence on the reduction of contrast volume and the possible reduction of contrast-induced nephropathy (CIN) by the utilization of ACIs compared to manual injection. Several studies report the effects of ACIs on the volume of contrast used during coronary angiography; fewer studies examine the effects of contrast volume on renal function. We hypothesized that 1) contrast sparing devices reduce total contrast volume utilized during diagnostic and interventional cases; and 2) through the reduction of contrast volume, CIN is also reduced.

Methods

We searched MEDLINE (through April 2013), ClinicalTrials.gov, and The Cochrane Library, for clinical trials comparing ACIs versus manual injection and whether contrast media volume and/or rates of CIN were reported. As of April, 2013, 62 potentially relevant articles were identified. We also did a manual search on cross-references which were included in this meta-analysis.

Key word MESH terms included “automated injection”, “manual injection”, “automated contrast injectors” and “ACIST” for the ACIST Injection System (ACIST™; ACIST Medical Systems, Eden Prairie, Minnesota). Studies were included if they compared the amount of contrast volume delivery between ACIs and manual manifold injection systems in patients undergoing diagnostic coronary angiography and/or ad hoc PCI. Exclusion criteria included the absence of a manual injection arm or failing to report delivered contrast volume. Data was abstracted following appropriate methods according to the Quality of Reporting of Meta-analysis statement.(10) Two authors (K.M. and H.K.) independently reviewed the articles and recorded information outcomes on spreadsheets. Study quality was assessed by Jadad criteria (Table 1).(11)

Summary statistics were calculated using Cochrane Collaborative software, RevMan5.4.1 (Baltimore, M.D.). We tested for heterogeneity by using the I^2 test.(12) Heterogeneity was observed in the diagnostic and diagnostic and ad hoc comparisons. Therefore a random effects model was used to account for the existing heterogeneity across the studies. Weighted

mean difference (MD) and 95% confidence intervals (CI) were calculated for contrast volume delivered and fluoroscopy time. Methods for the calculation have been previously described.

Results

We retrieved 62 articles that report on cardiac catheterization, ACIs, prevention of CIN, the use of contrast in other diagnostic cardiac modalities including magnetic resonance imaging and angiography. Forty-two articles were excluded as they did not meet inclusion criteria or report on coronary angiography. Twenty studies were reviewed for more detailed information, and 10 withdrawn as they did not include a comparison arm or report on contrast volume (Figure 1). Jadad scores ranged between 0 and 2 (Table 2).

Ten studies met our inclusion criteria and are included in this analysis (Table 2).(1-9, 13) A total of 79,694 patients were included: 20,099 patients in the ACI arm and 59,595 patients in the manual contrast injection arm. Demographics were similar among all studies and there were no gender related differences. Six studies were randomized controlled trials, 3 studies were retrospective cohorts, and one study divided patients based on the preference of the intervening cardiologist. Three different procedures were performed on patients including diagnostic coronary angiography, diagnostic angiography with ad hoc PCI, and PCI only (Figure 2).

Overall, contrast volume was reduced by 45 ml (Figure 2) when using ACIs compared to manual injection. The incidence of CIN was reduced in the ACI group by 15% (Figure 3). ACIs resulted in a non-significant reduction in CIN in diagnostic coronary angiography and ad hoc PCI, and a non-significant reduction of in PCI alone.

Discussion

We conducted a meta-analysis to evaluate contrast volume administered via ACI systems compared to manual injection. Overall, ACIs reduced contrast volume delivery by 45 ml and in reduced CIN by 15%.

ACIs have been reported to deliver less contrast volume during cardiac catheterization while maintaining image quality. It is likely that the reduction in contrast volume delivered using ACIs may reduce the patient's risk for CIN.(14-16) As shown by Call and colleagues there were 108 ml [-127, -89] less contrast used by ACIs with a 31.1% relative reduction in the incidence of CIN when ACIs were used for diagnostic catheterization and ad hoc PCI.(3) Incidence of CIN was reduced in the ACI group with an overall odds ratio of 0.85 ($p<0.001$, 95% CI: 0.78, 0.93, Figure 3). ACIs resulted in a non-significant reduction in CIN with an odds ratio of 0.81 ($p =0.16$, 95% CI, 0.60, 1.08) in diagnostic coronary angiography, a significant reduction of 0.75 ($p<0.001$, 95% CI, 0.63, 0.90) in diagnostic procedures and PCI, and a non-significant reduction of 0.90 ml ($p = 0.08$, 95% CI, 0.80, 1.01) in PCI only, when compared to a manual manifold. The precise pathophysiology has not been established, though contrast media-induced renal vasoconstriction, direct tubular toxicity, lipid peroxidation, and erythrocyte aggregation may be underlying mechanisms.(14)

Four studies compared outcomes based on catheter size; only one compared 4F catheters used in both arms, and 3 reported differences between 6F catheters used in manual manifold systems compared with 4F catheters used with ACIs.(4, 6-8) One study concluded no difference in the amount of contrast volume delivery, while 3 reported significantly less contrast volume use when using the 4F automated injection compared with manual technique.(4, 6, 7) Overall, 5.53 ml ($p = 0.01$, 95% CI, -9.91, -1.16) less contrast was delivered in the ACIST group compared to the manual group employing automated injectors for left ventriculography only. However, our meta-analysis does not have the ability to explore the causal role of catheter size on contrast volume or CIN endpoints.

There are some limitations to consider. First, the majority of the constituent patient population was derived from 2 studies; 1 study utilized retrospective data from patients that had received manual injection before ACIs had been employed at their hospital, thus the majority of the cohort was in the manual injection group.(5, 13) The other study does not report whether patients were randomized.(13) Larger populations give greater weight when employing a fixed effects model. Additionally, lack of randomization allows for methodological biases and confounding variables including the use of catheter size and biplane to reduce contrast use. Two studies are a continuation of each other, the only difference being 5 additional patients included in the manual injection group.(4, 7) However, after excluding the second study with 5 additional patients, we determined that there were still statistically significant lower volumes of contrast administered for diagnostic catheterizations. Second, the nature of the studies do not allow for equipoise or blinding; 2 studies report randomization techniques, 1 of which employed a faulty strategy, and none report withdrawal or dropout rates, creating an overall low Jadad score (Table 2). Despite lack of blinding we do not believe that study methodology affects the validity of this analysis.

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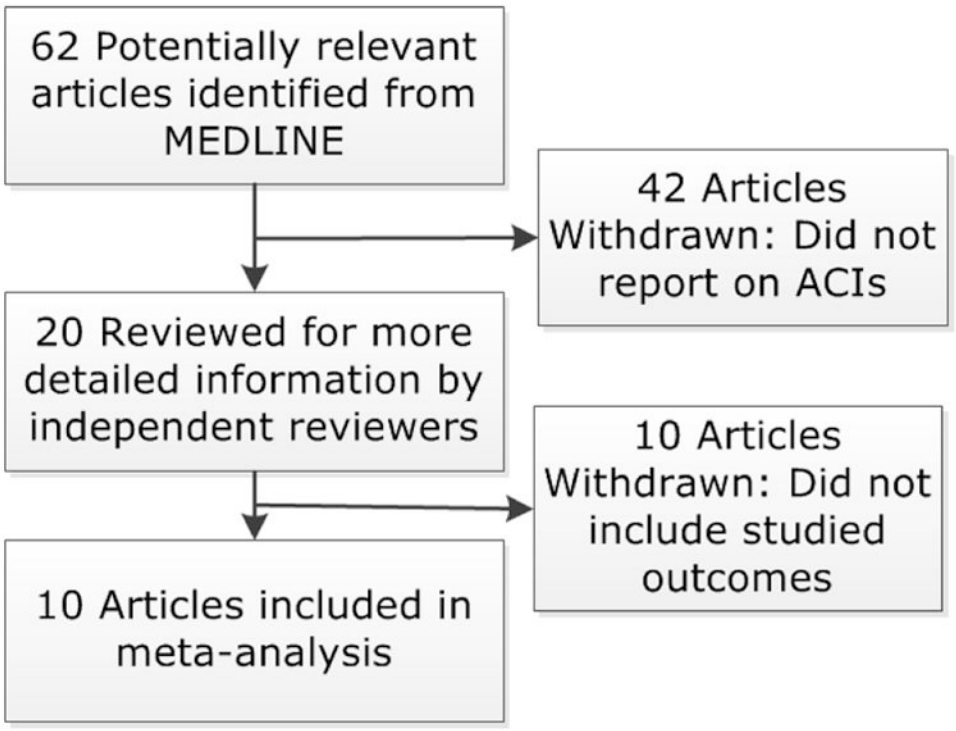

Figure 1. Selection of Studies

The figure flow diagram documents the flow of relevant study identification and the selection process for review and final inclusion in the meta-analysis.

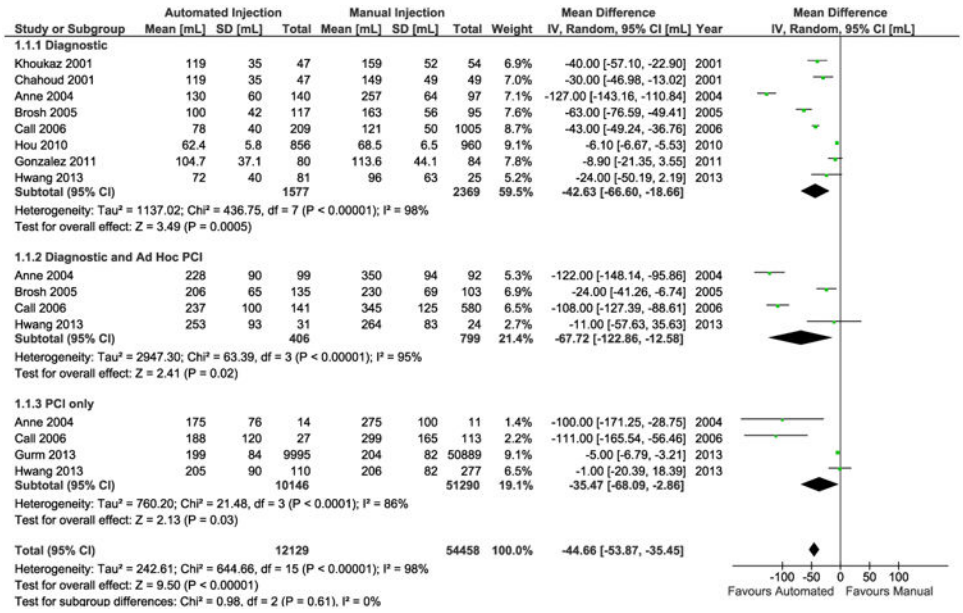

Figure 2. Meta-analysis of Contrast Volume Use

The forest plot graphs the weighted mean difference in contrast volume use between manual injection and ACIs devices stratified by type of procedure each with a sub-group summary estimate (black diamond) and a final summary estimate at the bottom for all types of procedure. The small boxes and horizontal lines depict the weighted mean difference for contrast volume for each listed study.

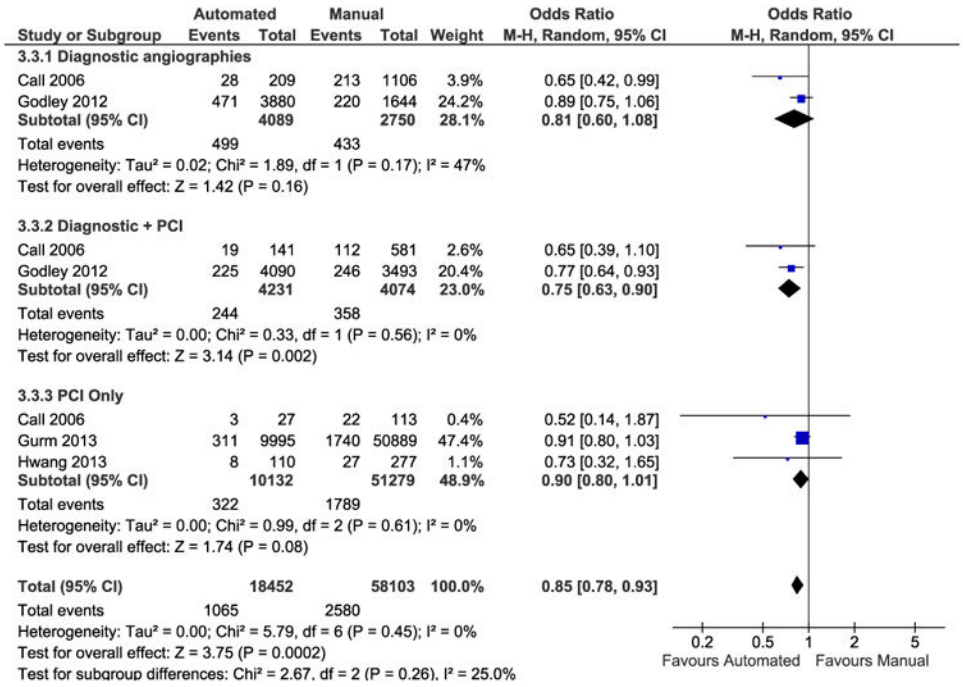

Figure 3. Meta-analysis of Contrast-induced Nephropathy

The forest plot graphs the odds ratios for CIN between manual injection and ACIs devices stratified by type of procedure each with a sub-group summary estimate (black diamond) and a final summary estimate at the bottom for all types of procedure. The small boxes and horizontal lines depict the odds ratio and 95% confidence intervals for CIN nephropathy for each listed study.

Table 1

Study Characteristics

Article	Reference Number	Intervention	N	Protocol	Enrollment criteria	Study Type	RCT	Jadad Score
Anne et al. 2004	6	Automated Injection	253	Contrast injection with ACIST device	Catheterization and/or PCI	Prospective	+	2
		Manual Injection	200	Manual contrast injection using stopcock-manifold system				
Brosh et al. 2005	4	Automated Injection	117	Contrast injection with ACIST device	Catheterization and angiography or PCI		+	1
		Manual Injection	95	Manual injection with hand syringe				
Call et al. 2006	5	Automated Injection	377	Automated contrast injection	Catheterization and PCI	Retrospective observational	0	1
		Manual Injection	1,798	Manual injection with hand syringe				
Chahoud et al. 2001	7	Automated Injection	47	Contrast injection using 4Fr ACIST device	Catheterization and coronary arteriography	Prospective	+	1
		Manual Injection	49	Manual injection with 4Fr catheter				
Godley et al. 2012	16	Automated Injection	7,970	Contrast injection using ACIST device	Catheterization and ad hoc PCI	Retrospective observational	0	1
		Manual Injection	5,137	Manual injection				
Gonzalez et al. 2010	11	Automated Injection	80	Contrast injection using 4Fr catheter	Catheterization	Prospective	+	1
		Manual Injection	84	Manual injection with 6Fr catheter				
Gurm et al. 2013	8	Automated Injection	9,995	Automated injection with ACIS; catheter size per operator preference	PCI	Propensity matching retrospective observational	0	1
		Manual Injection	50,889	Manual injection; catheter size per operator preference				
Hwang et al. 2013	12	Automated Injection	306	Contrast injection using Avanta Fluid Management Injection System	Catheterization and ad hoc PCI	Prospective	+	1
		Manual Injection	1,052	Manual injection with				
Hou et al. 2010	9	Automated Injection	856	Contrast injection using 4Fr ACIST device	Coronary angiography	Prospective	0	0
		Manual Injection	960	Manual injection with 6Fr catheter				
Khoukaz et al. 2001	10	Automated Injection	47	Contrast injection using 4Fr ACIST device	Catheterization and coronary arteriography	Prospective	+	1
		Manual Injection	46	Manual injection with 6Fr catheter				