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Contemporary use of and outcomes associated with ultra- low contrast volume in patients undergoing Percutaneous Coronary Interventions

Running Title: Ultra-low contrast volume and outcomes

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This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1002/ccd.27819

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Word Count: 4130

Abstract

Background: The risk of Contrast Induced Acute Kidney Injury (CI-AKI) increases in a non-linear fashion with increasing volume of contrast media. Prior studies recommend limiting contrast volume to less than 3 times the estimated creatinine clearance (CC). Recently, a number of operators have reported successful percutaneous coronary intervention (PCI) using even lower volumes of contrast.

Objectives: To evaluate the prevalence and outcomes associated with ultra-low contrast volume among patients undergoing PCI.

Methods: We assessed the prevalence of, and outcomes associated with use of ultra-low contrast volume among 75,393 patients undergoing PCI in Michigan between July 2014 and June 2017 in the BMC2 (Blue Cross Blue Shield of Michigan Cardiovascular Consortium) registry. Ultra-low contrast volume was defined as contrast volume less than or equal to the patient's estimated CC. Patients receiving dialysis at the time of the procedure were excluded.

Results: Ultra-low contrast volume was used in 13% of procedures with the majority of these patients being at low risk of renal complications. Compared with patients who received a contrast volume between one to three times the CC, use of ultra-low volume of contrast was associated with a significantly lower incidence of AKI (aOR 0.682, 95% CI 0.566 – 0.821, P <

0.001) and a lower incidence of need for dialysis (aOR = 0.341, 95% CI 0.165 – 0.704, p = 0.003). These benefits were most evident in the patients with a high baseline predicted risk of AKI.

Conclusions: A small but clinically significant number of patients are treated with ultra-low contrast volume. Ultra-low contrast volume use is associated with a significant reduction in the incidence of AKI or need for dialysis. It may be prudent to consider this new threshold when performing PCI on patients who are at an increased risk of AKI.

Keywords:
Percutaneous Coronary Intervention (PCI)
Comparative Effectiveness/Patient Centered Outcomes Research
Complications, PCI
Contrast Agent
Health Care Outcomes
Renal Disease, Chronic

Abbreviations & Acronyms:
PCI = Percutaneous Coronary Intervention
CC = Creatinine Clearance
CI-AKI = Contrast-induced acute kidney injury

Introduction

Contrast Induced Acute Kidney injury (CI-AKI) is a common complication of invasive cardiac procedures and is associated with increased morbidity, mortality and health care cost (1,2). Use of low-osmolar or iso-osmolar contrast media, contrast volume minimization and appropriate hydration are the only evidence-based strategies that have been effective at reducing the incidence of CI-AKI (3,4). Current professional society recommendations focus on identification of high-risk patients, appropriate peri-procedural hydration and minimization of contrast volume in high-risk patients as strategies to prevent CI-AKI(5). In prior work, our group and others have suggested a benefit of renal function-based contrast media dosing with a contrast dose of less than 3 times the estimated creatinine clearance (CC) being associated with a low incidence of CI-AKI(6,7).

The increasing awareness of the association of contrast media volume with the risk of CI-AKI appears to have resulted in a change in practice towards using lower doses of contrast media for all patients (8) . In addition, select centers have reported their experience with performing PCI with ultra-low volume of contrast media, especially in high-risk patients (9,10) .

The prevalence and clinical impact of this practice in the broader interventional community remains unknown. Our study had two aims. First, we sought to identify the prevalence of ultra-low contrast use in a broad and unselected population of patients undergoing PCI in Michigan using the BMC2 (Blue Cross Blue Shield of Michigan Cardiovascular Consortium) registry, a large multicenter quality improvement collaborative. Second, we assessed the impact of ultra-low contrast volume administration on reducing the risk of acute kidney injury (AKI), and need for dialysis.

Materials and Methods

Study population

Our study population was comprised of all patients undergoing PCI between July 1, 2014 and June 30, 2017 at every nonfederal hospital in the state of Michigan and enrolled in the BMC2 registry. This registry has been previously described in detail elsewhere (11,12). BMC2 is a quality improvement collaborative of all non-federal hospitals that perform PCI in the state of Michigan that works to facilitate inter institutional quality improvement. A total of 47 hospitals participate in the registry, of which 14 perform PCI without on-site cardiac surgery backup. Procedural data on all patients undergoing PCI at participating hospitals are collected using NCDR Cath PCI data collection system with additional data elements collected using a BMC2 website. Baseline data include clinical, demographic, procedural, and angiographic characteristics, as well as pharmacotherapy used before, during, and after the procedure, and in-hospital outcomes. All data elements are prospectively defined, and a rigorous study coordinator training and education program is in place to ensure high data quality. All study sites are audited at least once a year by an experienced nurse auditor.

We excluded patients who were on dialysis at the time of the procedure, those who died in the catheterization laboratory, those undergoing salvage PCI, those who underwent coronary artery bypass grafting during the same hospitalization, those missing pre-procedural or post-procedural creatinine values, and those in whom glomerular filtration rate or baseline AKI risk could not be estimated due to missing information.

We defined ultra-low contrast volume as a contrast dose less than or equal to the calculated creatinine clearance (CC). In a previous modelling study, this threshold appeared to be associated with a statistically lower adjusted risk of renal complications (13). High contrast volume was defined as a contrast dose > 3X CC. Low contrast volume was defined as a contrast dose that was greater than the CC but less than or equal to three times the CC.

Study endpoints. This study had two end points, AKI and the new need for dialysis. Acute kidney injury was defined as a post PCI elevation in serum creatinine of ≥0.5 mg/dL above the pre- PCI value. We and others have previously demonstrated this definition to be preferable to more sensitive definitions of AKI for predicting the likelihood of hard clinical events (14,15). Peak creatinine was defined as the highest value of creatinine in the week after the procedure and was ascertained as per local clinical practice. A follow-up creatinine was collected at least 1 day after the procedure but varied, depending on length of stay. The CC was calculated with the Cockcroft-Gault equation (16). Cockcroft-Gault equation was used for assessment of renal function adjusted contrast dose since this estimate has been conventionally used for renal dosing of medications, and has been used in prior work describing renal function based contrast thresholds (6,17).

Statistical analysis

Pearson Chi-Square tests were utilized for comparisons of categorical variables, and Student t-tests for comparisons of continuous variables between cases with CV/CC <= 1 (Ultra-low volume) and cases with CV/CC between 1 and 3 (low volume). Pre-procedural risk of AKI was estimated using the BMC2 risk prediction model, which has been described previously (18) and is implemented as an online calculator (available for review at http://scaipciriskapp.org/pci_welcome).

Logistic regression models adjusting for estimated pre-procedural AKI risk were utilized to assess the impact of contrast volume indexed to creatinine clearance on AKI incidence. The extent to which the effect of contrast volume varied by baseline AKI risk was assessed through the inclusion of risk category (<1%, 1-7%, and >7% baseline predicted AKI risk) by ultra-low contrast interaction terms, and the likelihood ratio test was used to determine whether the addition of an estimated risk by ultralow contrast interaction term significantly improved the fit of the model. The regression model was then utilized to determine number needed to treat (NNT) adjusting for estimated pre-procedural AKI risk. Using the fitted model, two predicted AKI rates were obtained. First, we predicted AKI rate if all patients in the study cohort received ultra-low contrast volume (AKI rate a). We then predicted the AKI rate if all patients were to have received low contrast volume (AKI rate b). NNT was then estimated as the inverse of the difference of the two predicted rates (NNT = 1/(b-a)).

Logistic regression was utilized to determine patient baseline clinical and demographic characteristics independently associated with ultra-low contract use, with all variables having absolute standardized differences between ultralow contrast cases and either low or high contrast volume use cases of 10% or greater evaluated as predictors, variables having coefficients with Wald p-values of alpha = .05 or less were considered to be independent predictors. To determine the extent that ultra-low contrast volume use varied between hospitals or PCI operators after accounting for patient factors, a generalized linear mixed effect regression model was fitted adjusting for patient level independent predictors as fixed effect terms, and including random intercept terms for unique hospitals and operators. The median odds ratio (MOR) statistics was estimated from this model, with a 95% confidence interval obtained using a parametric bootstrap procedure iteratively drawing from the estimated posterior distributions of the random effects(19).MOR estimates reflect the extent of intra-site and intra-operator contribution to overall variance in the use of ultra-low contrast volume. All analyses were performed using R version 3.4.1.

Results

A total of 91,945 patients underwent PCI during the 3 years of the study period of whom 75,393 comprised our study population (supplementary figure 1). The average contrast volume was

171 ml with a median contrast volume of 160 ml (IQR 120-209 ml). The distribution of CC adjusted contrast dose in the total cohort is provided in figure 1. Ultra-low contrast volume was used in 13 % of patients during this study period. The baseline characteristics of the cohort categorized by CV/CC of <=1 (ultra-low volume), CV/CC>1-3 (low volume) and CV/CC > 3 (high volume) are provided in table 1. There were multiple statistically significant but clinically minor differences between those treated with ultra-low contrast volume compared with those administered larger contrast dose. Compared with patients treated with low contrast volume, those treated with ultra-low contrast were more likely to be younger, taller and of greater body weight and more likely to be undergoing radial access and had a lower serum creatinine at baseline. The calculated risk of AKI was 2.09% in those treated with ultralow contrast volume compared with 2.62 % in those treated with a low contrast volume.

The distribution of ultralow volume contrast use among patients at varying risk of AKI and by baseline renal function are provided in supplementary figure 2. The majority of patients who were treated with ultra-low contrast volume were at low risk of AKI (60% had a predicted risk of < 1%).

The unadjusted and risk adjusted incidence of AKI in the entire cohort categorized by CV/CC is provided in figure 2. There was an increase in the risk of AKI with increasing renal function adjusted contrast dose. When categorized by the predicted risk of AKI, the advantage of ultra-low contrast volume was most evident in the highest risk cohort (Figure 3).

In a logistic regression model adjusting for estimated baseline risk of AKI, ultra-low contrast volume was associated with a lower incidence of AKI compared with those administered a low contrast volume (OR 0.682, 95% CI 0.566 – 0.821, $P < 0.001$). The addition of a predicted risk by ultra-low contrast interaction term significantly improved the fit of the regression model, with the effect of ultra-low contrast increasing with greater baseline AKI risk. (LRT = 4.32 on 1 df, $p = 0.038$). The NNT for avoiding one AKI event with use of ultra-low contrast volume compared with a low dose was 410 for patients with a predicted risk of AKI of < 1% (low risk), 246 for intermediate risk group and 18 for the high-risk cohort (predicted risk > 7%).

In subsequent stratified analysis of cases where predicted AKI risk was > 7%, ultralow contrast volume was associated with lower AKI incidence after adjusting for baseline BMC2 estimated AKI risk (OR = 0.673, 95% CI 0.511 – 0.887, $p = 0.005$).

The total number of patients who needed dialysis was low: 9/9,857 (0.091%) in those treated with ultra-low volume contrast, 113/51,584 (0.219%) in those receiving a low volume and 189/13,952 (1.35%) in those administered a high volume (Chi-Square $p = 0.009$ for ultra-low volume versus low volume, and $p< 0.001$ for ultra-low versus high volume). After adjusting for the baseline predicted risk of dialysis, the use of ultra-low volume contrast was a significantly associated with lower odds of new need for dialysis (OR = 0.34, 95% CI 0.17 – 0.70, $p = 0.003$ for ultra-low volume vs low volume, and OR = 0.14, 95% CI 0.07 – 0.30, $p < 0.001$, for ultra-low volume vs high volume).

There was significant difference in the use of ultra –low contrast volume across the individual operators and the participating institutions (figure 4). The independent predictors of ultra-low volume contrast use are provided in supplementary table 1. After adjusting for patient level factors, there was a large persistent difference in the use of ultralow contrast among the participating operators (supplementary figure 3) and the participating institutions (supplementary figure 4). The MOR for operators was 1.85 (1.78 – 1.92) and for institutions 1.62 (95%CI: 1.52 – 1.73) suggesting that a similar patient was 1.85 fold more likely to receive ultra-low contrast depending on the operator and 1.62 fold depending on the treating institution. By comparison, the model predicted odds ratio associated with a 10 -point increase in patient GFR was 1.47, and for a 10 year decrease in patient age was 1.49 (all else held constant), suggesting that institutional and operator effects are comparable in scope to important differences in patient presentation in terms of the likelihood that ultra-low contrast volume would be administered.

Discussion

The key finding of our study is that the use of ultra-low volume contrast is increasingly being adopted in the broader interventional community and is associated with a meaningful reduction in the risk of AKI among high-risk patients. The use of CV/CC ratio is a simple tool that may be helpful in guiding contrast dosing in patients undergoing PCI. In our prior work, the risk of AKI and need for dialysis was markedly increased when the CV/CC ratio exceeded 3. Our findings corroborate and significantly extend the findings by focusing on the other end of the spectrum of contrast use and demonstrate significant improvement in outcome with use of ultralow volume contrast especially in high-risk patients. Because creatinine clearance is routinely calculated for patients undergoing invasive cardiac procedures, and the use of CV/CC ratio is increasingly being incorporated into clinical practice, clinical adoption of our current findings should be relatively straightforward.

The morbidity and health care cost associated with CI-AKI has been described by many investigators (1). Both in-vivo data and clinical studies have demonstrated an association between high contrast volume and the risk of AKI(20,21). Various different contrast thresholds have been described and collaborative efforts to reduce the proportion of patients exceeding these thresholds have been associated with a reduction in the incidence of AKI(22-24). In a recent study, we described the trends in contrast use over a 7-year period in Michigan(8). There was a steady decline in the average contrast volume per procedure over the study period with the mean contrast volume declining from 197 (75) ml in calendar year 2010 to 168 (75) ml in calendar year 2016. There was a substantial decline in the proportion of patients exceeding CV/CC ≥3 with a commensurate reduction in the risk adjusted incidence of AKI.

While these efforts have focused on avoiding high volumes of contrast media, many groups have focused on performing PCI with exceedingly low volume of contrast. One of the earliest such report was from Kane and colleagues who described their experience with ultra-low volume of contrast use in a cohort of 185 patients with National Kidney Foundation stages 3 to 5 chronic, non-dialysis-dependent kidney disease treated at the Mayo clinic. This study demonstrated both the feasibility of such an approach in a larger cohort and the associated reduction in the incidence of AKI with use of lower volumes of contrast media(9). An approach for minimizing contrast volume to less than 15 ml was reported by Nayak and colleagues who described their strategy of routine biplane angiography, use of adjunctive imaging such as intravascular ultrasound (IVUS) guidance, "dry" fluoroscopic imaging, and careful minimization of the contrast injection in the highest risk patients(10). These benefits of using IVUS guidance to minimize contrast media volume have been further validated in a randomized trial by Mariani and colleagues. (25). This field has been further extended by the pioneering work of Ali and colleagues who have reported on a series of patients on whom they were able to perform PCI without using any contrast media whatsoever (26). More recently, studies of the Dyevert ™ system (Osprey Medical Inc., Minnetonka, MN, USA) have demonstrated clinically and statistically significant reductions in the volume of contrast media administered during coronary angiography and/or interventions (27,28).

These studies reflect the experience of select quaternary care institutions and the broad uptake of these approaches in the broader community has previously not been explored. Our work suggests that a select group of operators across multiple hospitals are adopting the principle of ultralow volume contrast. Paradoxically, a majority of patients who were treated with low volume contrast were at low risk of AKI and this may simply reflect the adoption of an "*As low as reasonably achievable* (ALARA)" approach to contrast dosing. More importantly, the use of ultra-low contrast media, was associated with meaningful reduction in the incidence of AKI in high-risk patients. While association cannot be used to ascribe causality, the observed differences in the incidence of AKI with use of ultra-low contrast volume suggests that broader adoption of this approach needs to be explored.

A key finding of our study was that the strongest predictor of ultra-low contrast volume was the operator and to a lesser extent the institution performing the procedure. This suggests that there may be opportunities to both selectively refer high-risk patients to operators and institutions that are more likely to use ultra-low volume of contrast as well as to train operators more broadly on the principles of ultra-low volume contrast use. Furthermore, we believe, that such metrics should be, in general, shared with high-risk patients undergoing non-emergent PCI as part of better informed consent process.

Highest-risk patients make up 12.5% of the total population undergoing PCI in our cohort and had 63.4 % of the total CI-AKI events. Future quality improvement efforts focused on broader utilization of ultra-low volume contrast in this population are needed to assess if this approach will result in reduced morbidity and health care cost.

Study limitations

The BMC2-PCI registry is a regional database from the state of Michigan with an active focus on multicentric quality improvement and might or might not be representative of the wider population of patients undergoing PCI. The collaborative has been focused on use of renal function-based contrast thresholds and this metric is tracked quarterly by all participating hospitals. Our findings, however reflect the work across the entire state of Michigan and comprise the experience of both academic and community hospitals and make our findings more generalizable. Data were limited to in-hospital information, serum creatinine was not collected in a standardized fashion, and only the highest post-PCI value was recorded. It is likely that a number of patients were discharged before peaking of the serum creatinine, and our study might underestimate the occurrence of AKI. Our study is observational in nature and cannot ascribe causality.

Conclusion

A small but significant proportion of patients undergoing PCI are treated with ultra-low low volume of contrast. The use of ultra-low volume of contrast is associated with a reduction in the risk of AKI especially in the highest-risk patients. Further studies are warranted to explore broader utilization of this threshold in high-risk patients undergoing PCI.

Funding:

This work was supported by the Blue Cross Blue Shield of Michigan and Blue Care Network as part of the Blue Cross Blue Shield of Michigan Value Partnerships program. The funding source supported data collection at each site and funded the data-coordinating center but had no role

in study concept, interpretation of findings, or in the preparation, final approval or decision to submit the manuscript.

Acknowledgements:

The authors are indebted to all the study coordinators, investigators, and patients who participated in the BMC2 registry.

Disclaimer:

Although Blue Cross Blue Shield of Michigan (BCBSM) and BMC2 work collaboratively, the opinions, beliefs and viewpoints expressed by the author do not necessarily reflect the opinions, beliefs and viewpoints of BCBSM or any of its employees.

Conflict of Interest:

Hitinder S. Gurm receives research funding from Blue Cross Blue Shield of Michigan, the National Institutes of Health and is a consultant for Osprey Medical. P. M Grossman receives research funding from NIH and Blue Cross Blue Shield of Michigan and is a consultant for Medtronic cardiovascular. Thomas A. LaLonde is on the Speakers Bureau for AstraZeneca for ticagrelor. Louis A Cannon is on the Scientific Advisory Boards of Boston Scientific, Medtronic, and Abbott ST Jude. Ryan D. Madder receives research support from Infraredx and Corindus Vascular Robotics. None of the authors have any conflicts directly relevant to this study.

Authors' Contributions:

Hitinder Gurm and Milan Seth had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Seth, Gurm

Acquisition, analysis, or interpretation of data: Dixon, LaLonde, Sukul, Gurm

Drafting of the manuscript: Gurm

Critical revision of the manuscript for important intellectual content: Dixon, LaLonde, West, Lauver, Cannon, Madder, Grossman

Statistical analysis: Seth

Obtained funding: Gurm

Study supervision: Gurm

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Figure Legends

1. Figure 1: Distribution of PCI procedures by ratio of Contrast volume to Creatinine clearance.

2. Figure 2: Unadjusted and Risk Adjusted incidence of AKI by categories of Contrast Volume/creatinine clearance.
3. Figure 3: Risk adjusted AKI rates by CV/CC categories and pre-procedural predicted risk of AKI.
4. Figure 4: Use of ultra-low volume contrast as a proportion of all cases performed by an operator or at a participating institution in Michigan.
5. Supplementary Figure 1: Flow Diagram of Study Population.
6. Supplementary Figure 2: Distribution of contrast volume/creatinine clearance (CV/CCC) categorized as <1 (ultra-low), >1 to 3 (low), and >3 (high) among patients categorized by predicted risk of AKI and by pre-procedural glomerular filtration rate (GFR).
7. Supplementary Figure 3: A caterpillar plot depicting the substantial variation in the log odds of ultra-low volume contrast use across interventional cardiologists in Michigan.
8. Supplementary Figure 4: A caterpillar plot depicting the variation in the log odds of ultra-low volume contrast use across the participating hospitals in Michigan.

Tables

Table 1: Baseline characteristics, procedural variables and key in-hospital outcomes of the cohort categorized by contrast volume to creatinine clearance ratio.

Supplementary Table: Independent predictors of Ultra-low contrast Volume.

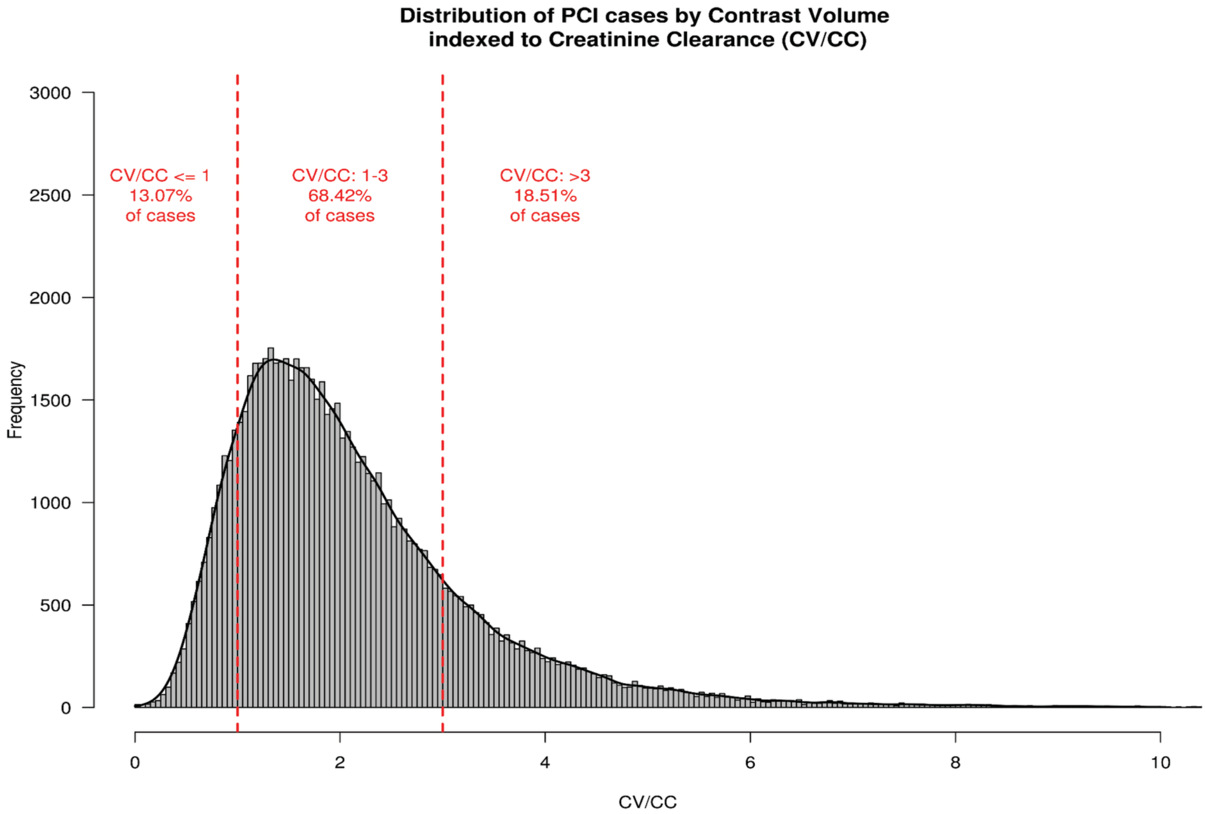

Figure 1: Distribution of PCI procedures by ratio of Contrast volume to Creatinine clearance

Figure 1.tif

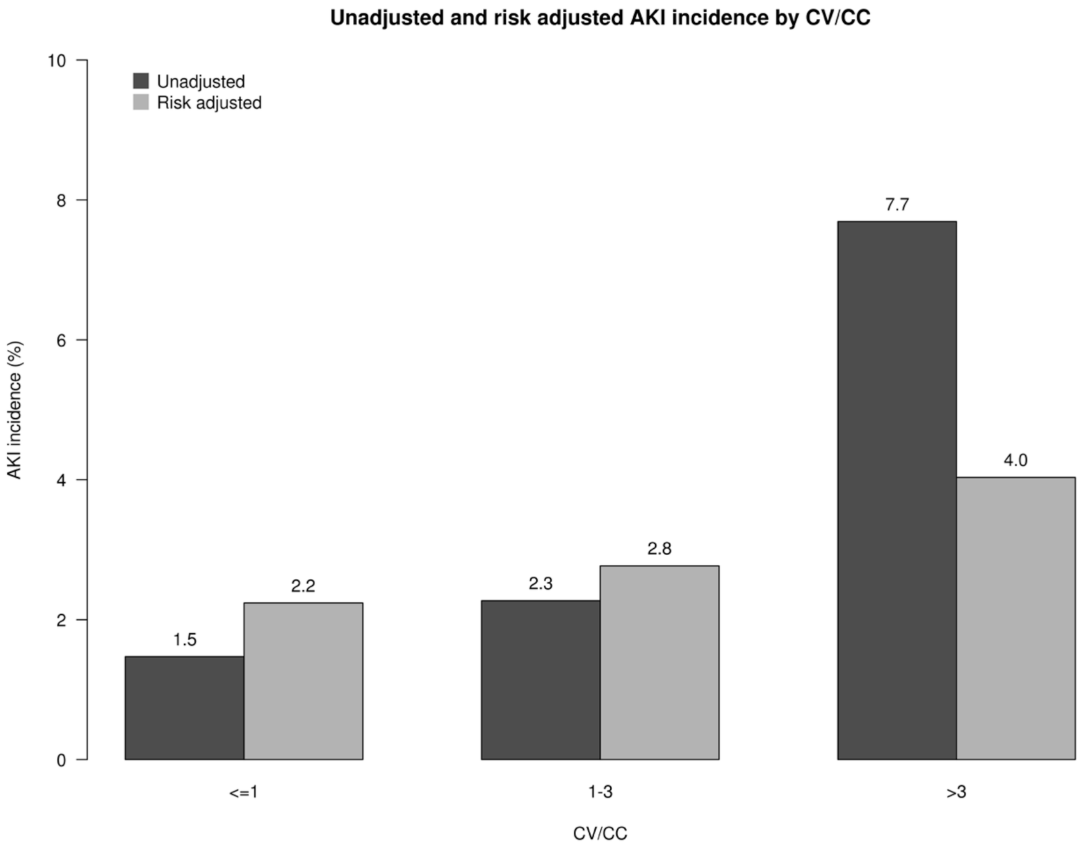

Figure 2: Unadjusted and Risk Adjusted incidence of AKI by categories of Contrast Volume/creatinine clearance.

Figure 2.tif

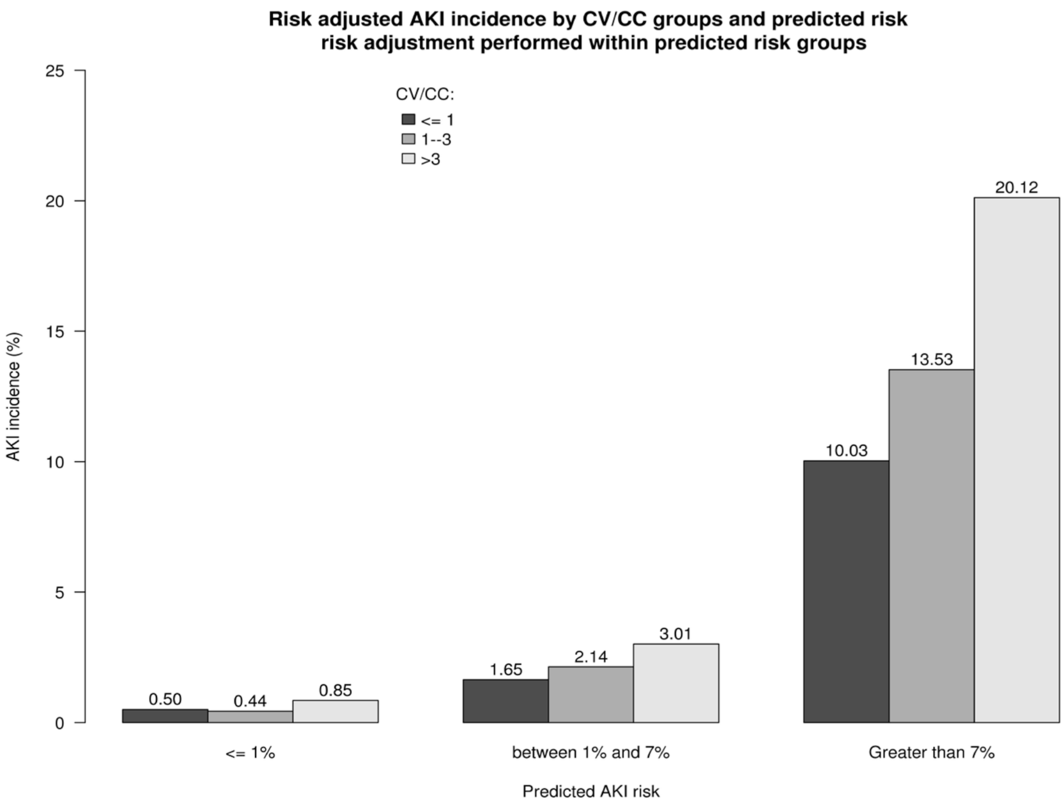

Figure 3: Risk adjusted AKI rates by CV/CC categories and pre-procedural predicted risk of AKI.

Figure 3.tif

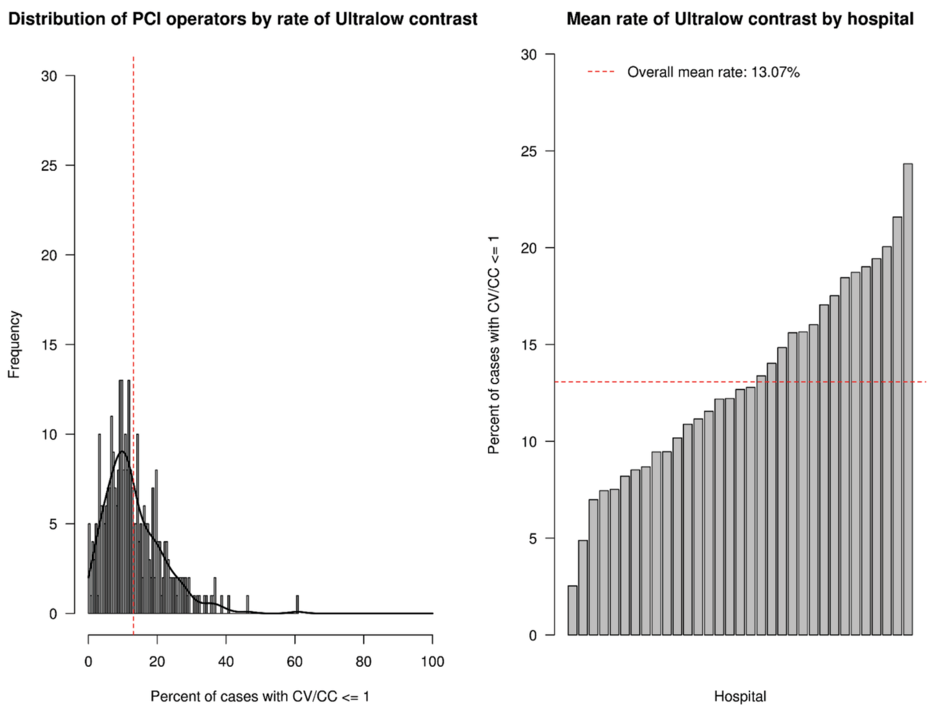

Figure 4: Use of ultralow volume contrast as a proportion of all cases performed by an operator or at a participating institution in Michigan.

Figure 4.tif

	Contrast Volume group				Ultra-low contrast volume compared to low contrast volume			Ultra-low contrast volume compared to high contrast volume	
Characteristic	Ultra-low (CV/CC <= 1)	Low (CV/CC: >1-3)	High (CV/CC > 3)		p-value	Abs. Std. diff		p-value	Abs. Std. diff
Demographic Characteristics									
Age (years)	57.49 ± 10.85	64.93 ± 11.21	74.38 ± 10.46		p < 0.001	67.37		p < 0.001	158.5
Height (cms)	173.34 ± 10.54	171.74 ± 10.34	167.92 ± 10.56		p < 0.001	15.34		p < 0.001	51.4
Weight (kg)	103.06 ± 24.85	90.77 ± 20.21	77.84 ± 17.61		p < 0.001	54.23		p < 0.001	117.1
Sex: Male	6,872/9,857 (69.7%)	35,653/51,584 (69.1%)	8,017/13,952 (57.5%)		p = 0.237	1.30		p < 0.001	25.7
Sex: Female	2,985/9,857 (30.3%)	15,931/51,584 (30.9%)	5,935/13,952 (42.5%)		p = 0.237	1.30		p < 0.001	25.7
Race - White	8,496/9,857 (86.2%)	44,915/51,584 (87.1%)	12,006/13,952 (86.1%)		p = 0.018	2.58		p = 0.758	0.4
Race - Black or African American	1,128/9,857 (11.4%)	5,530/51,584 (10.7%)	1,642/13,952 (11.8%)		p = 0.034	2.30		p = 0.441	1.0
Race - Asian	102/9,857 (1.0%)	582/51,584 (1.1%)	175/13,952 (1.3%)		p = 0.418	0.90		p = 0.120	2.1
Race - American Indian or Alaskan Native	46/9,857 (0.5%)	176/51,584 (0.3%)	33/13,952 (0.2%)		p = 0.057	1.98		p = 0.002	3.9
Race - Native Hawaiian or Pacific Islander	11/9,857 (0.1%)	33/51,584 (0.1%)	10/13,952 (0.1%)		p = 0.105	1.61		p = 0.307	1.3
Hispanic or Latino Ethnicity	157/9,815 (1.6%)	672/51,303 (1.3%)	205/13,889 (1.5%)		p = 0.023	2.42		p = 0.445	1.0
Admit Source: Emergency department	4,380/9,846 (44.5%)	22,792/51,537 (44.2%)	6,111/13,942 (43.8%)		p = 0.633	0.52		p = 0.317	1.3
Comorbidities, Risk Factors and Clinical Presentation									
Current/Recent Smoker (w/in 1 year)	3,734/9,855 (37.9%)	14,970/51,568 (29.0%)	2,647/13,948 (19.0%)		p < 0.001	18.86		p < 0.001	42.9
Hypertension	8,181/9,856 (83.0%)	43,480/51,582 (84.3%)	12,534/13,949 (89.9%)		p = 0.001	3.48		p < 0.001	20.1
Dyslipidemia	7,685/9,849 (78.0%)	40,911/51,553 (79.4%)	11,293/13,947 (81.0%)		p = 0.003	3.25		p < 0.001	7.3
Family History of Premature CAD	1,709/9,856 (17.3%)	6,912/51,577 (13.4%)	1,228/13,949 (8.8%)		p < 0.001	10.94		p < 0.001	25.5
Prior MI	3,485/9,856 (35.4%)	17,464/51,580 (33.9%)	4,986/13,951 (35.7%)		p = 0.004	3.16		p = 0.546	0.8

Prior Heart Failure	1,403/9,853 (14.2%)	8,672/51,579 (16.8%)	3,550/13,947 (25.5%)		p < 0.001	7.11		p < 0.001	28.4
Prior Valve Surgery/Procedure	115/9,853 (1.2%)	932/51,567 (1.8%)	452/13,947 (3.2%)		p < 0.001	5.29		p < 0.001	14.2
Prior PCI	4,623/9,857 (46.9%)	23,324/51,579 (45.2%)	6,302/13,951 (45.2%)		p = 0.002	3.37		p = 0.008	3.5
Cerebrovascular Disease	1,056/9,854 (10.7%)	7,576/51,582 (14.7%)	3,101/13,949 (22.2%)		p < 0.001	11.95		p < 0.001	31.4
Peripheral Arterial Disease	990/9,854 (10.0%)	7,090/51,582 (13.7%)	2,916/13,951 (20.9%)		p < 0.001	11.44		p < 0.001	30.4
Chronic Lung Disease	1,663/9,855 (16.9%)	9,769/51,581 (18.9%)	3,251/13,948 (23.3%)		p < 0.001	5.39		p < 0.001	16.1
Diabetes Mellitus	4,229/9,853 (42.9%)	19,813/51,576 (38.4%)	5,436/13,951 (39.0%)		p < 0.001	9.18		p < 0.001	8.1
CAD Presentation: No symptom, no angina	371/9,855 (3.8%)	1,536/51,575 (3.0%)	410/13,950 (2.9%)		p < 0.001	4.36		p < 0.001	4.6
CAD Presentation: Symptom unlikely to be ischemic	221/9,855 (2.2%)	1,353/51,575 (2.6%)	442/13,950 (3.2%)		p = 0.028	2.47		p < 0.001	5.7
CAD Presentation: Stable angina	812/9,855 (8.2%)	4,782/51,575 (9.3%)	1,189/13,950 (8.5%)		p = 0.001	3.65		p = 0.437	1.0
CAD Presentation: Unstable angina	4,305/9,855 (43.7%)	22,089/51,575 (42.8%)	5,687/13,950 (40.8%)		p = 0.116	1.72		p < 0.001	5.9
CAD Presentation: Non-STEMI	2,687/9,855 (27.3%)	13,171/51,575 (25.5%)	3,731/13,950 (26.7%)		p < 0.001	3.92		p = 0.373	1.2
CAD Presentation: ST-Elevation MI (STEMI) or equivalent	1,459/9,855 (14.8%)	8,644/51,575 (16.8%)	2,491/13,950 (17.9%)		p < 0.001	5.37		p < 0.001	8.3
Heart Failure w/in 2 Weeks	1,056/9,849 (10.7%)	6,364/51,561 (12.3%)	2,822/13,943 (20.2%)		p < 0.001	5.08		p < 0.001	26.5
Cardiomyopathy or Left Ventricular Systolic Dysfunction	799/9,854 (8.1%)	5,042/51,579 (9.8%)	2,003/13,944 (14.4%)		p < 0.001	5.84		p < 0.001	19.9
Pre-operative Evaluation Before Non-Cardiac Surgery	149/9,856 (1.5%)	867/51,578 (1.7%)	262/13,951 (1.9%)		p = 0.228	1.35		p = 0.033	2.8
Cardiogenic Shock w/in 24 Hours	93/9,856 (0.9%)	731/51,580 (1.4%)	509/13,951 (3.6%)		p < 0.001	4.39		p < 0.001	18.1
Cardiac Arrest w/in 24 Hours	124/9,853 (1.3%)	980/51,573 (1.9%)	365/13,951 (2.6%)		p < 0.001	5.15		p < 0.001	9.9
Procedural Characteristics									
Fluoroscopy Time	11.27 ± 8.36	15.67 ± 11.61	23.44 ± 17.74		p < 0.001	43.48		p < 0.001	87.8
Contrast Volume	106.58 ± 41.19	168.08 ± 58.37	228.61 ±		p < 0.001	121.73		p < 0.001	184.9

			83.76						
IABP	105/9,857 (1.1%)	825/51,575 (1.6%)	561/13,952 (4.0%)		p < 0.001	4.66		p < 0.001	18.9
Other Mechanical Ventricular Support	48/9,857 (0.5%)	532/51,569 (1.0%)	504/13,951 (3.6%)		p < 0.001	6.28		p < 0.001	22.2
Arterial Access Site: Femoral	4,922/9,857 (49.9%)	31,489/51,579 (61.1%)	10,584/13,952 (75.9%)		p < 0.001	22.51		p < 0.001	55.7
Arterial Access Site: Brachial	20/9,857 (0.2%)	98/51,579 (0.2%)	38/13,952 (0.3%)		p = 0.789	0.29		p = 0.284	1.4
Arterial Access Site: Radial	4,908/9,857 (49.8%)	19,946/51,579 (38.7%)	3,322/13,952 (23.8%)		p < 0.001	22.53		p < 0.001	55.9
Arterial Access Site: Other	7/9,857 (0.1%)	46/51,579 (0.1%)	8/13,952 (0.1%)		p = 0.574	0.64		p = 0.679	0.5
PCI Status: Elective	2,700/9,857 (27.4%)	15,124/51,584 (29.3%)	3,900/13,952 (28.0%)		p < 0.001	4.28		p = 0.341	1.3
PCI Status: Urgent	5,600/9,857 (56.8%)	26,993/51,584 (52.3%)	7,249/13,952 (52.0%)		p < 0.001	9.02		p < 0.001	9.8
PCI Status: Emergency	1,557/9,857 (15.8%)	9,467/51,584 (18.4%)	2,803/13,952 (20.1%)		p < 0.001	6.80		p < 0.001	11.2
Pre-PCI Left Ventricular Ejection Fraction	52.98 ± 11.92	51.87 ± 12.94	49.44 ± 14.56		p < 0.001	8.97		p < 0.001	26.6
Chronic Total Occlusion PCI	150/9,588 (1.6%)	1,353/50,563 (2.7%)	627/13,637 (4.6%)		p < 0.001	7.7		p < 0.001	17.6
Bifurcation PCI	495/9,588 (5.2%)	3,997/50,563 (7.9%)	1,565/13,637 (11.5%)		p < 0.001	11.1		p < 0.001	23.0
Left Main artery PCI	160/9,588 (1.7%)	1,428/50,563 (2.8%)	863/13,637 (6.3%)		p < 0.001	7.8		p < 0.001	24.0
Atherectomy	106/9,588 (1.1%)	993/50,563 (2.0%)	496/13,637 (3.6%)		p < 0.001	7.0		p < 0.001	16.7
Cardiogenic Shock at Start of PCI	97/9,850 (1.0%)	782/51,566 (1.5%)	556/13,946 (4.0%)		p < 0.001	4.79		p < 0.001	19.4
Laboratory Values									
Pre-Procedure Creatinine	0.85 ± 0.30	1.02 ± 0.33	1.32 ± 0.68		p < 0.001	52.72		p < 0.001	89.0
Pre-Procedure Hemoglobin	13.76 ± 1.89	13.58 ± 1.92	12.75 ± 2.05		p < 0.001	9.66		p < 0.001	51.5
Creatinine Clearance (Cockcroft – Gault)	143.1 ± 54.7	95.3 ± 34.7	56.5 ± 22.0		p < 0.001	104.30		p < 0.001	207.50
Pre-procedural estimated AKI risk (%)	2.09 ± 4.27	2.62 ± 4.59	5.59 ± 7.83		p < 0.001	12.11		p < 0.001	61.5
Key In-hospital Outcomes									

Dissection	47/9,853 (0.5%)	368/51,562 (0.7%)	207/13,946 (1.5%)		p= 0.0086	3.1		p< 0.0001	10.2
Stent thrombosis	13/9,857 (0.1%)	81/51,580 (0.2%)	"20/13,952 (0.1%)		p= 0.5583	0.7		p= 0.8149	0.3
Post-Procedure Creatinine	0.87 ± 0.35	1.02 ± 0.44	1.37 ± 0.91		p < 0.001	36.85		p < 0.001	73.0
Post-Procedure Hemoglobin	12.90 ± 1.84	12.52 ± 1.91	11.34 ± 2.11		p < 0.001	20.47		p < 0.001	78.6
Myocardial Infarction (Biomarker Positive)	107/9,849 (1.1%)	906/51,557 (1.8%)	403/13,945 (2.9%)		p < 0.001	5.67		p < 0.001	12.9
Cardiogenic Shock	73/9,850 (0.7%)	790/51,557 (1.5%)	618/13,946 (4.4%)		p < 0.001	7.47		p < 0.001	23.4
Heart Failure	147/9,850 (1.5%)	1,384/51,558 (2.7%)	925/13,946 (6.6%)		p < 0.001	8.34		p < 0.001	26.3
CVA/Stroke	11/9,850 (0.1%)	150/51,559 (0.3%)	120/13,945 (0.9%)		p = 0.001	4.00		p < 0.001	10.8
Tamponade	5/9,850 (0.1%)	42/51,557 (0.1%)	45/13,945 (0.3%)		p = 0.313	1.19		p < 0.001	6.3
AKI	145/9,857 (1.47%)	1,172/51584 (2.27%)	1,073/13,952 (7.69%)		p < 0.001	5.91		p < 0.001	30.1
New Requirement for Dialysis	9/9,850 (0.1%)	113/51,559 (0.2%)	189/13,945 (1.4%)		p = 0.009	3.25		p < 0.001	15.0
Other Vascular Complications Requiring Treatment	34/9,850 (0.3%)	219/51,559 (0.4%)	119/13,945 (0.9%)		p = 0.259	1.29		p < 0.001	6.6
RBC/Whole Blood Transfusion	86/9,849 (0.9%)	801/51,558 (1.6%)	784/13,945 (5.6%)		p < 0.001	6.22		p < 0.001	27.0
Bleeding Event w/in 72 Hours	193/9,850 (2.0%)	1,816/51,558 (3.5%)	1,173/13,946 (8.4%)		p < 0.001	9.58		p < 0.001	29.4
Discharge Status: Alive	9,821/9,857 (99.6%)	51,174/51,584 (99.2%)	13,457/13,952 (96.5%)		p < 0.001	5.66		p < 0.001	23.1
Discharge Status: Deceased	36/9,857 (0.4%)	410/51,584 (0.8%)	495/13,952 (3.5%)		p < 0.001	5.66		p < 0.001	23.1