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Clinical Research

Clinical Decision Support to Reduce Contrast-Induced Kidney Injury During Cardiac Catheterization: Design of a Randomized Stepped-Wedge Trial

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ABSTRACT

Background: Contrast-induced acute kidney injury (CI-AKI) is a common and serious complication of invasive cardiac procedures. Quality improvement programs have been associated with a lower incidence of CI-AKI over time, but there is a lack of high-quality evidence on clinical decision support for prevention of CI-AKI and its impact on processes of care and clinical outcomes.

Methods: The **C**ontrast-**R**educing **I**njury **S**ustained by **K**idneys (Contrast RISK) study will implement an evidence-based multifaceted intervention designed to reduce the incidence of CI-AKI, encompassing automated identification of patients at increased risk for CI-AKI, point-of-care information on safe contrast volume targets, personalized recommendations for hemodynamic optimization of intravenous fluids, and follow-up information for patients at risk. Implementation will use cardiologist academic detailing, computerized clinical decision

RÉSUMÉ

Contexte : La néphropathie provoquée par un produit de contraste (NPPC) est une complication grave et fréquente des interventions cardiaques invasives. Les programmes d'amélioration de la qualité ont été associés à une diminution de la fréquence de la NPPC au fil du temps. Cependant, il y a un manque de données probantes de grande qualité au regard de l'aide à la décision clinique pour la prévention de la NPPC et des répercussions de celle-ci sur les processus de soins et les résultats cliniques.

Méthodologie : L'étude Contrast RISK (*Contrast-Reducing Injury Sustained by Kidneys*) permettra de mettre en œuvre une intervention multifacette fondée sur des données probantes et conçue pour réduire la fréquence de la NPPC. Cette intervention comprendra le repérage automatisé des patients exposés à un risque accru de NPPC; l'accès à de l'information sur les volumes cibles sécuritaires de produits de

Contrast-induced acute kidney injury (CI-AKI) remains a common and serious adverse complication following cardiac catheterization and percutaneous coronary intervention (PCI).[1-4] More than 1300 patients (9% of all procedures) develop CI-AKI following diagnostic coronary angiography or PCI in Alberta, Canada each year. These patients experience a median 3-day increase in hospital stay, a 50% increase in the risk of hospital readmission, and a clinically significant 3% increase in the risk of kidney failure requiring dialysis.[5,6] The health care system shoulders an additional CAN $3700 to $22,000 cost per patient with CI-AKI because of these events.[7-9]

Strategies that may reduce the incidence of CI-AKI include preprocedural assessment of CI-AKI risk,[10-13] minimization of iodinated radiocontrast media during procedures,[14-18] and intravenous hydration before and immediately after the procedure.[19-21] Unfortunately, consistent uptake of these strategies is highly variable.[1,22,23] Quality improvement programs for CI-AKI prevention that systematically incorporated CI-AKI prevention strategies have reported a reduction in the

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support, and audit and feedback. All 31 physicians practicing in all 3 of Alberta's cardiac catheterization laboratories will participate using a cluster-randomized stepped-wedge design. The order in which they are introduced to this intervention will be randomized within 8 clusters. The primary outcome is CI-AKI incidence, with secondary outcomes of CI-AKI avoidance strategies and downstream adverse major kidney and cardiovascular events. An economic evaluation will accompany the main trial.

Conclusions: The Contrast RISK study leverages information technology systems to identify patient risk combined with evidence-based protocols, audit, and feedback to reduce CI-AKI in cardiac catheterization laboratories across Alberta. If effective, this intervention can be broadly scaled and sustained to improve the safety of cardiac catheterization.

contrastel à où les soins sont dispensés; des recommandations personnalisées pour l'optimisation hémodynamique des fluides administrés par voie intraveineuse; et des renseignements sur le suivi dans le cas des patients à risque. La mise en œuvre de l'intervention fera appel à une présentation faite en milieu d'enseignement par un cardiologue, à un système informatisé d'aide à la décision clinique ainsi qu'à un processus de vérification et de rétroaction. Les 31 médecins qui exercent dans les trois laboratoires de cathétérisme cardiaque de l'Alberta y participeront, suivant un plan d'étude aléatoire par grappes et par étapes. Les médecins seront répartis aléatoirement dans huit grappes, dans l'ordre de présentation de l'intervention. La fréquence de la NPPC est le paramètre d'évaluation principal. Les stratégies d'évitement de la NPPC et les événements rénaux et cardiovasculaires indésirables majeurs en aval constituent les paramètres d'évaluation secondaires. L'essai principal s'accompagnera d'une évaluation économique.

Conclusions : L'étude Contrast RISK met à contribution des systèmes de technologie de l'information pour cerner les risques auxquels les patients sont exposés — parallèlement à des protocoles fondés sur des données probantes et à un processus de vérification et de rétroaction — en vue de réduire la fréquence de la NPPC dans l'ensemble des laboratoires de cathétérisme cardiaque de l'Alberta. Si elle s'avère efficace, cette intervention pourra être déployée et soutenue à grande échelle en vue d'assurer une mise en œuvre plus sécuritaire du cathétérisme cardiaque.

relative risk of CI-AKI by 20% and achieved an incidence of CI-AKI of only 4%[24,25] but have not been widely disseminated or adopted.

The **Contrast** **R**educing **I**njury **S**ustained by **K**idneys (Contrast RISK) initiative aims to implement a multifaceted intervention systematically and consistently to support evidence-based strategies to reduce the incidence of CI-AKI in Alberta. This pragmatic trial uses a cluster-randomized stepped-wedge design to deliver education, clinical decision support, and audit and feedback reports to all cardiologists performing cardiac catheterization and PCI in Alberta. This article describes the design and rationale of the Contrast RISK initiative, including the intervention components, methods of implementation, and analytical considerations for its evaluation.

Methods

Participants and settings

Sites and workflow differences. The initiative includes all 3 cardiac catheterization laboratories in the province of Alberta. All sites use the Alberta Provincial Project for Outcomes Assessment in Coronary Heart Disease (APPROACH; www.approach.org) electronic clinical information system.[26] Details on how the initiative was adapted for implementation in each centre are in the Supplementary Material.

Recruitment of cardiologists and allied health providers. All 31 interventional and diagnostic cardiologists at the three cardiac catheterization laboratories in Alberta were approached for inclusion in the study. At each site, an interventional cardiologist has been designated as the site-lead, serves as a member of the steering committee, and piloted the decision support tools before the initiation of the trial. Individual cardiology physicians at each centre are approached for inclusion in the intervention by their site-lead and receive information on endorsement of the study by their site medical director, local catheterization laboratory manager, and provincial leadership (Directors of Alberta Health Services Cardiovascular Health Strategic Clinical Network [SCN] and Kidney Health SCN). Registered nurses, medical radiation technologists (MRTs) and physiology technicians, and other allied health care providers in the 3 cardiac catheterization units also receive education and training on the intervention.

Patient inclusion and exclusion criteria. All Albertan residents above the age of 18 undergoing diagnostic or therapeutic coronary angiography in Alberta are considered for inclusion; however, patients receiving dialysis at the time of catheterization and those undergoing emergency primary PCI for ST-elevation myocardial infarction (STEMI) are excluded owing to an inability to detect possible postprocedural declines accurately in kidney function among those on dialysis and the time-sensitive nature of STEMI procedures.

Intervention

CI-AKI prevention: intervention components. The Contrast RISK trial includes interventions to promote uptake of 4 evidence-based strategies for assessing and minimizing the risk of CI-AKI:

Automated identification of patients at increased-risk of CI-AKI. Identifying preprocedural patient risk may promote the use of procedural strategies and postprocedural follow-up to reduce the risk of CI-AKI. Risk-prediction models simultaneously

incorporate prognostic factors to provide personalized estimates of patient absolute risk of CI-AKI.[10-13] External validation of 7 risk prediction models for CI-AKI in Alberta identified a model particularly well suited for clinical implementation because of better discrimination, calibration, accuracy of risk stratification, and feasibility based on readily available patient data.[27] This model has been integrated into the existing APPROACH electronic system without refitting or recalibration to provide personalized, preprocedural CI-AKI risk estimates for patients. The study population includes all patients with model-predicted risk of CI-AKI above 5%, which includes the 25% to 30% (290 to 360 patients per month) of the eligible population receiving cardiac procedures in Alberta. Patients whose model-predicted risk is below 50% are expected to have a much higher number needed to treat and were excluded from the group eligible for the intervention so that maximal attention could be focused on those more likely to benefit.

Point-of-care clinical decision support to recommend safe contrast volume targets. Reducing the amount of contrast dye delivered can reduce the risk of developing CI-AKI.[15] Procedural tactics that reduce the volume of contrast delivered include the use of automated contrast injectors, biplane angiography, use of smaller syringes and catheters, avoiding left ventriculography, and staging PCI procedures for non-culprit arteries.[14-18] Safe contrast targets are calculated and displayed graphically in the APPROACH system before the initiation of arterial access for all patients above 5% risk of CI-AKI. Cardiologists may exceed the safe contrast target for a given case at their discretion.

Personalized recommendations for hemodynamic optimization of intravenous fluids. Intravenous (IV) fluid administration has been identified as an important element of CI-AKI prevention.[19-21] In the Prevention of Contrast Renal Injury With Different Hydration Strategies (POSEIDON) trial, left ventricular end diastolic pressure (LVEDP)-guided IV fluid administration safely increased the average volume of IV fluid administered to patients at increased risk and reduced the incidence of CI-AKI compared with conventional IV fluid-administration practices.[28] The decision support tools for the Contrast RISK initiative include an automated calculation of personalized IV fluid hydration rates according to the POSEIDON trial protocol. Patients with active or recent heart failure within 2 weeks of catheterization, severe valvular heart disease, or mechanical aortic valve are excluded from consideration for LVEDP-guided IV fluid administration owing to their high risk for volume overload with additional fluids and safety concerns related to crossing the aortic valve, respectively. The use of IV fluids and appropriate rates of administration will be left to the discretion of the treating physician for such patients.

Follow-up information provided to patients at above average or high risk. Follow-up laboratory testing for kidney function and electrolytes is required to identify patients with CI-AKI and ensure that they receive appropriate timely follow-up.[23,29-33] Through processes coordinated before discharge from each cardiac catheterization laboratory, patients at increased risk of CI-AKI, who are discharged the same day as their procedures, are provided with an information package for themselves and their primary care providers including instructions for oral hydration, follow-up, and a laboratory requisition for serum creatinine testing 48 to 72 hours postprocedure. Information for primary care physicians is designed to bridge transition to community care and includes a link to the online provincial clinical pathway for testing, management, and referral for kidney disease (http://www.ckdpathway.ca/). Postcatheterization and PCI orders have been modified to communicate the increased CI-AKI risk status of patients and facilitate ordering of the hemodynamic-guided fluids and serum creatinine. The Alberta Health Services laboratory database, which captures data from all inpatient and outpatient facilities in the province, will be used to audit completeness of laboratory follow-up and CI-AKI incidence.

Implementation processes

A user-acceptance testing process for the clinical decision support tool was conducted with end users—including each physician site-lead—to ensure that it was user friendly, fully functional, and could handle real-world clinical situations. Subsequently, a 3-month pilot-testing phase from November 2017, to January 2018, was completed with staff and the site-lead at each centre to ensure processes for using and communicating information from the decision support tools could be integrated into usual workflow at each of the sites.

Once scaled up to full implementation at each site, eligible patients have their CI-AKI risks estimated and recorded in the APPROACH system and receive the postprocedural follow-up pathway if they are identified to be at-risk. When physicians are introduced into the study according to the stepped-wedge design, they begin to receive information on CI-AKI risk status, safe contrast targets, and optimized IV fluid recommendations from that date forward.

Knowledge translation components

Educational outreach with academic detailing. Before the entry of physicians into the Contrast RISK intervention, educational sessions are provided to increase awareness about the risk of CI-AKI, introduce the evidence behind the strategies for reducing the risk of developing CI-AKI that form the core of the intervention, summarize how the intervention will be delivered within the catheterization unit work flow, describe the rationale behind a stepped-wedge design of the trial, facilitate understanding and uptake of the decision support tools, inform the continuous audit and feedback process, and confirm consent for ongoing participation.

Physician education is delivered through 1-on-1 or small-group (maximum 5 physicians per cluster) in-person sessions conducted by the site-lead with each participating cardiologist within 1 week before the date they begin receiving the intervention. Additional educational materials are available via a website (https://cumming.ucalgary.ca/contrast-risk/), including resources that summarize evidence, important aspects of the intervention, and protocol reference documents for each unit. Allied health staff—including nurses, MRTs, and physiology technicians—will be provided with group education through in-service sessions.

Computerized clinical decision support. Computerized clinical decision support includes CI-AKI risk prediction,

graphic display of safe contrast volume targets, and automated calculation of hemodynamic optimized IV fluid prescriptions (Fig. 1). Catheterization unit staff execute the CI-AKI risk prediction model upon completion of data entered in the APPROACH system, which is exchanged via an HL7 interface with Heath Outcomes Sciences ePRISM predictive analytics software hosted on the APPROACH servers.[34,35] Depending on site workflow, either an MRT or nurse inputs patient data for the 11 predictors included in the risk-prediction model and executes preprocedural calculation of the risk model, which classifies patients as low (below a predicted risk of 5%), above average (predicted risk 5% to 25%), or at high risk (predicted risk greater than 25% or a safe contrast target under 30 mL) of developing CI-AKI (Fig. 2).

Safe contrast targets are calculated with the ePRISM tool (Health Outcomes Sciences, Kansas City, Missouri), which employs a multivariable model developed from the National Cardiovascular Data Registry (NCDR) AKI risk model for estimating the optimal amount of contrast material needed to reduce the relative risk of CI-AKI by 15% for each patient, assuming a linear relationship between contrast volume and AKI risk when a patient's absolute risk of CI-AKI exceeds 5%.[36] With patients for whom an optimal contrast volume was calculated as < 30 cc, we have set a floor for reporting the limit as "30 cc or less." Safe contrast volumes are then displayed graphically in APPROACH for patients with calculated above average or high predicted risk of CI-AKI. Once randomized, cardiologists are alerted to this safe contrast target before the procedure and again when the safe contrast target has been reached. Contrast minimization strategies and indications for continuing procedures when the safe contrast targets are exceeded are recorded in the APPROACH system.

Hemodynamically optimized IV fluid recommendations are calculated automatically in the APPROACH system using LVEDP and weight and communicated to cardiologists during and following the procedure for patients who have had an LVEDP obtained and do not have recent heart failure. Should the cardiologist choose to order hydration differently, justification is requested and recorded.

Audit and feedback. Audit and feedback is provided to physicians every 3 months following their introduction to the intervention to maintain physician accountability by generating personalized reports for all cardiologists about their performance over fixed time intervals. The reports include contrast volume use administered relative to the safe contrast target, optimization of IV fluid to recommendations, and the CI-AKI incidence for patients at above average or high risk of CI-AKI (Fig. 3). The audit and feedback reports include physicians' performance relative to their site and provincial measures, along with recommendations for performance improvement. Site-leads will review this information with their peers.

Outcome measures

Primary and secondary outcomes. The primary outcome of the study is the incidence of CI-AKI, defined by an absolute increase in serum creatinine of $\geq$ 26 μmol/L (0.3 mg/dL) within 48 hours or a relative increase $\geq$50% within 4 days of procedure, based on Kidney Disease: Improving Global Outcomes (KDIGO) guidelines.[37] Alternative definitions of CI-AKI will be explored in sensitivity analyses (Table 1).

Secondary outcomes will be collected from existing data sources, including the APPROACH registry, Alberta Health administrative databases, Alberta Health Services laboratory database, Alberta Kidney Care North and South databases, and hospital electronic medical records (Table 1 and Supplemental Table S1). These outcomes include processes of care (volume of contrast-dye and IV fluids administered), mean bed days per patient managed, subsequent clinical events (cardiovascular events, kidney-specific events, and dialysis), patient-reported general (EQ-5D) and cardiovascular-specific (Seattle Angina Questionnaire) quality of life, estimated glomerular filtration rate (eGFR) 1 year after procedure, and economic costs. A cost-utility analysis will also be performed using provincial costing data from Alberta Health.

Blinding and randomization. The stepped wedge randomized trial designs involve sequential rollout of the intervention to clusters of physicians who perform cardiac catheterization or PCI in Alberta over a number of periods. By the end of the study, all participants will have received the intervention, with the order in which they started to receive the intervention determined at random. Given the nature of this intervention, it is neither possible to blind the physicians and associated health staff nor the members of the research team. Eight distinct clusters based on physician group (defined by location and practice group) with 3 to 5 physicians per cluster will be randomized to starting dates for the stepped-wedge design by a statistician using only non-identifiable physician numbers and blinded to the identity of the individual clusters (Fig. 4). Only the statistician and principal investigator will be aware of the order of the different clusters in advance, and unit staff and physicians will be blinded to the identity of the cluster until 1 month before their scheduled introduction date to provide appropriate time to enable education.

Statistical considerations

Study power. Observational studies of CI-AKI prevention initiatives have reported a 21% to 24% relative risk reduction in CI-AKI, which is a plausible and clinically important difference.[24,25] Data from the APPROACH registry was used to characterize a baseline 17% incidence of CI-AKI in patients at above average to high risk of CI-AKI in Alberta with an intracluster correlation among physicians for CI-AKI risk of 0.065 based on conventional models for stepped-wedge designs.[38,39] Based on inclusion of all cardiologists, 8 clusters, including a total of 31 physicians, will participate over the duration of the stepped-wedge trial. Current catheterization unit procedure volumes for the 3 centres ensures that 7270 above-average to high-risk patients in Alberta will be recruited over the 90-week duration of this trial (based on 10 weeks between entry of each of the 8 physician clusters to the intervention). Assuming the baseline CI-AKI incidence of 17% in eligible patients, a type I error rate of 5%, and the intracluster correlation between physicians of 0.065 (with corresponding design effect of 2.74), the study design provides more than 80% power to detect a

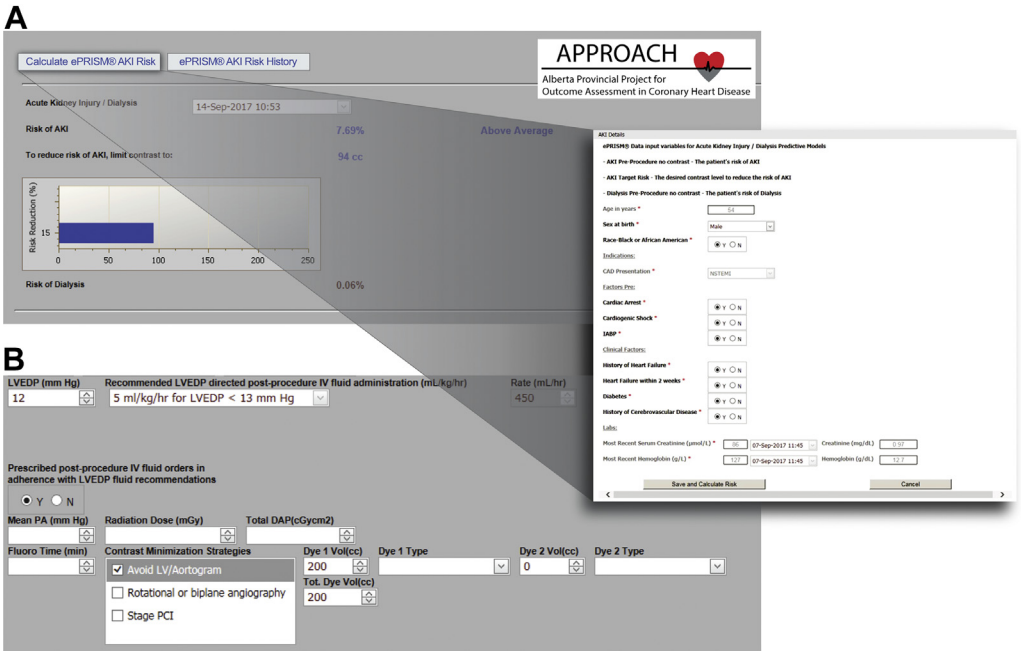

Figure 1. Electronic clinical decision support displays for contrast acute kidney injury risk prediction and prevention displayed in the Alberta Provincial Project for Outcomes Assessment in Coronary Heart Disease (APPROACH) system. (**A**) Acute kidney injury risk prediction and safe contrast target. (**B**) Hemodynamic optimized intravenous fluid recommendations.

3.9% absolute reduction and corresponding 22% relative reduction in risk of AKI.[40]

Descriptive analysis of the primary and secondary outcomes over the period of study will be presented at the patient level (eg, age, weight, proportion with heart failure), physician level (eg, mean volume of contrast and IV fluids ordered), and site level (eg, total number of PCIs conducted, incidence of CI-AKI). Mixed-effects regression models will be used for the analysis of pre- and postintervention differences in CI-AKI while controlling for time, patient-specific demographic and clinical characteristics, and site-level factors as fixed effects as delineated by Hussey and Hughes.[38,41] Patient-specific variation and between-site variations will be modelled as random effects. The secondary outcomes of processes of care, clinical,

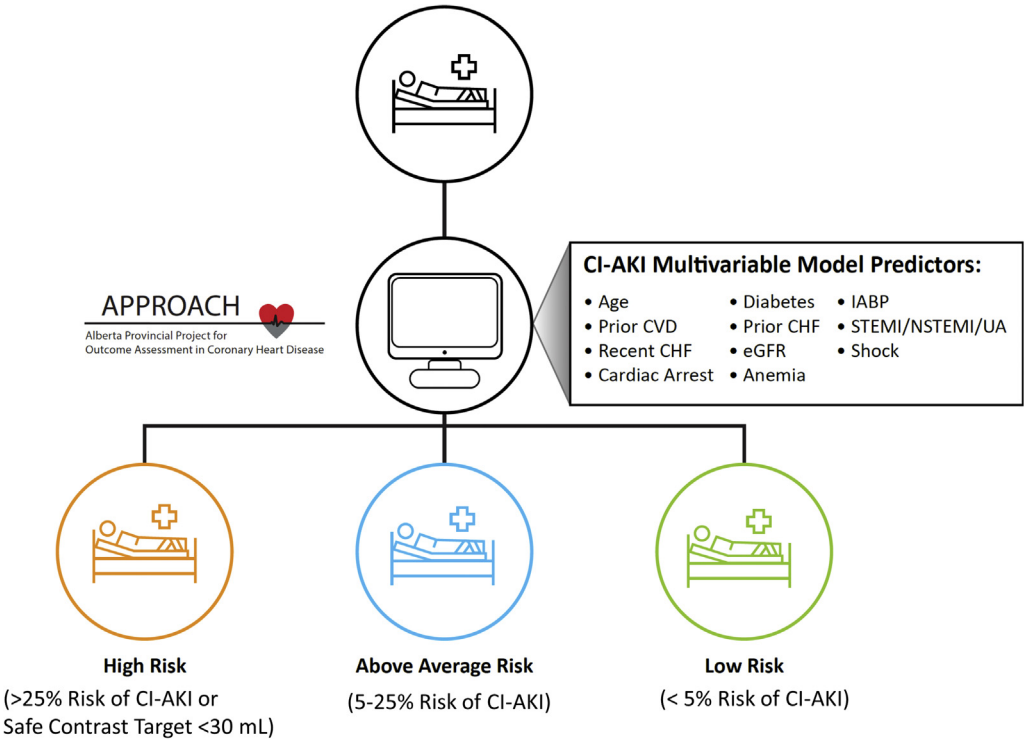

Figure 2. Risk stratification scheme for the randomized stepped-wedge trial to reduce contrast-induced injury sustained by kidneys during cardiac catheterization (**Contrast R**educing **I**njury **S**ustained by **K**idneys [Contrast RISK]).

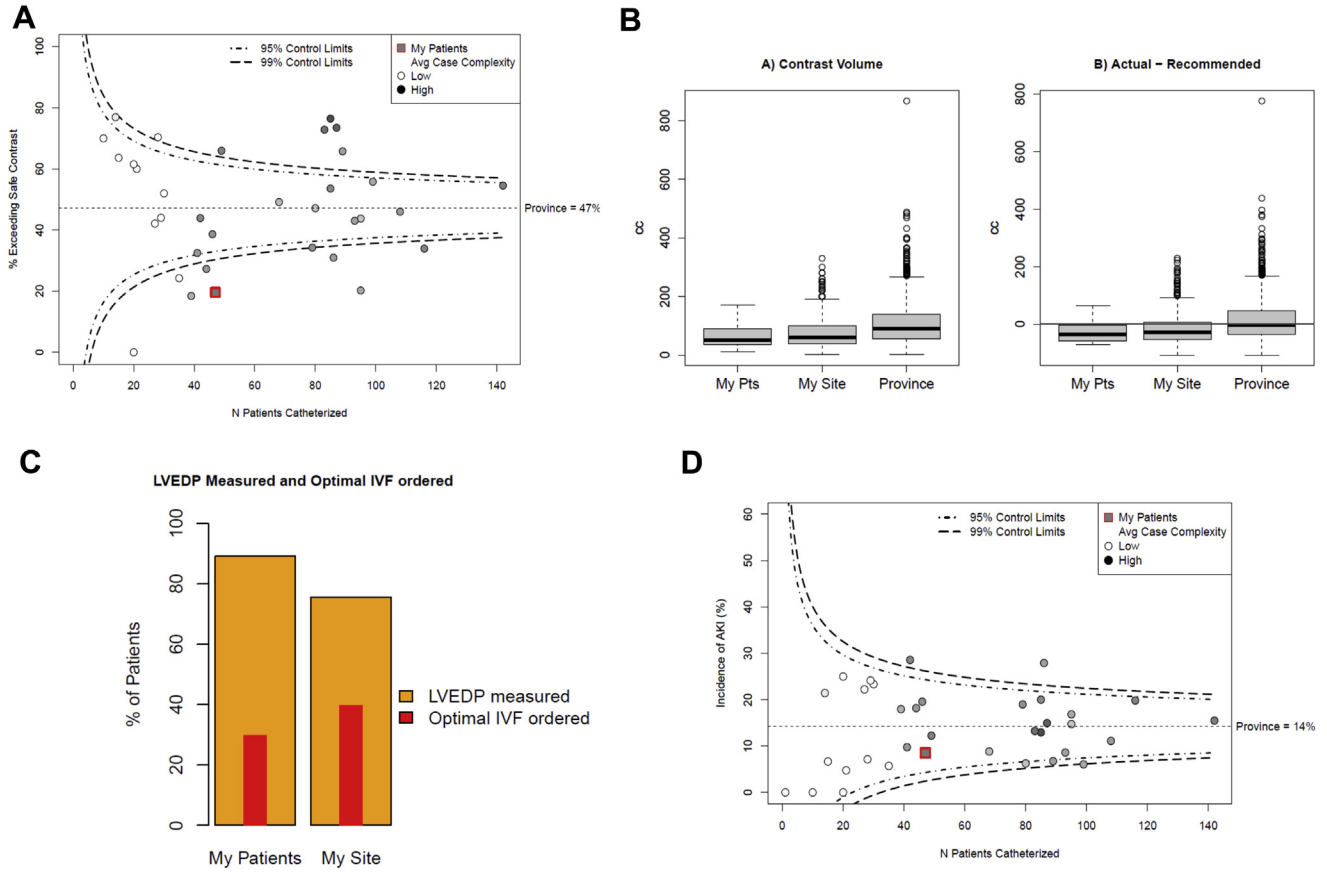

Figure 3. Audit and feedback report on process and outcomes measures in the randomized stepped-wedge trial to reduce contrast-induced injury sustained by kidneys during cardiac catheterization (**Contrast R**educing **I**njury **S**ustained by **K**idneys [Contrast RISK]). (**A**) Funnel plot of proportion of cases exceeding safe contrast target reported by physician. (**B**) Bar graphs of mean contrast volume used and mean difference between contrast volume used and target reported for a physician, site, and the province. (**C**) Bar graph of proportion of eligible patients with left ventricular end-diastolic pressure (LVEDP) measurement and with adherence to intravenous fluid recommendations. (**D**) Funnel plot of acute kidney injury incidence reported by physician.

and cost-related outcomes will be analyzed using the generalized mixed-effects regression model with an appropriate log link adjusting for similar covariates included in the analysis of the primary outcome. Sensitivity analyses will be performed to assess the impact of heterogeneity of pre- and postintervention differences across site and time. First, we will assess for heterogeneity of intervention effect across site in 2 ways: by checking for interactions between intervention and site as a fixed effect and by refitting the models with stratification according to site and comparing the intervention effects across sites (horizontal analysis). Second, we will assess for heterogeneity of intervention effect across time in 2 ways by checking for interactions between intervention and time point as a fixed effect and by refitting the models with stratification according to time point and comparing the intervention effect across time points.

Discussion

Assumptions underlying Contrast RISK effectiveness

AKI continues to be the most common noncardiac complication of PCI and can be reduced through quality improvement efforts. A systematic review of clinical decision support systems identified that such tools are often substantially more successful at improving clinical care practices when they are computer based and automatically provide decision support as part of existing clinician workflow at the time of decision making. In addition, the provision of a recommended course of action, rather than just a simple assessment of risk, increases the tool's likelihood of success.[42] Contrast RISK incorporates these aspects to maximize effectiveness; the computerized tool is embedded within existing cardiac catheterization laboratory workflow, information is relayed to the cardiologist at the time of decision making, and targets accompanied by recommendations on how to limit the volume of contrast and optimize fluid therapy are delivered at the point of care.

Regardless, successful translation of evidence-based strategies that reduce CI-AKI to clinical practice is dependent upon certain additional assumptions, including the intervention is correctly delivered to above-average and high-risk patients, safe contrast limits and IV fluid recommendations are consistently followed, audit and feedback findings are incorporated by physicians into their practice, and behavioural changes are sustained for the duration of the intervention.

Table 1. Study outcome definitions for the randomized stepped-wedge trial to reduce contrast-induced injury sustained by kidneys during cardiac catheterization (Contrast RISK)

Outcome	Definition	Source
Primary		
CI-AKI	Absolute increase in serum creatinine of $\geq$ 26 μmol/L (0.3 mg/dL) within 48 hours or a relative increase $\geq$ 50% within 4 days of procedure	AHS laboratory database
Secondary		
CI-AKI: alternate definitions	Absolute increase in serum creatinine of $\geq$ 26 μmol/L (0.3 mg/dL) within 48 hours Relative increase $\geq$50% within 4 days of procedure Absolute increase in serum creatinine of $\geq$ 44 μmol/L (0.5 mg/dL) within 48 hours or a relative increase $\geq$ 25% within 4 days of procedure	AHS laboratory database
Process Measures		
Contrast volume use	Mean volume of contrast used for each case	APPROACH database
Cases exceeding safe contrast target	Proportion of cases exceeding the safe contrast target by 30 cc or more	APPROACH database
Contrast-minimization strategies	Proportion of cases incorporating a contrast minimization strategy (avoidance of left-ventriculogram, staged procedure, biplane or rotational angiography)*	APPROACH database
IV fluid use	Mean volume of intravenous crystalloid used for prevention with each case	Hospital electronic medical records and charts
Cases receiving optimized IV fluid	Proportion of cases that received recommended intravenous fluids, based on weight and LVEDP	APPROACH database
Clinical Outcomes		
Postprocedural hospital bed days	Number of days in hospital including postprocedure length of stay plus readmissions up to 30 days after procedure	AH hospitalization database
Change in eGFR	Change in eGFR at 1 year from preprocedural baseline eGFR (estimated using CKD-EPI equation)	AHS laboratory database
Heart failure	Heart failure acquired during hospitalization for cardiac catheterization and/or PCI	AHS hospitalization database
Cardiovascular events	Hospital admission for angina, myocardial infarction, heart failure, or unplanned revascularization procedure (excluding staged procedures) within 1 year after procedure	AH hospitalization database and APPROACH database
Kidney events	Hospital admission with acute kidney injury or dialysis within 1 year after procedure	AH hospitalization and physician databases, Alberta Kidney Care North and South databases
End-stage kidney disease	Kidney failure requiring dialysis, kidney transplantation, or conservative management of kidney failure with eGFR $<$ 10 mL/min/1.73 m^2 within 1 year after procedure	AH hospitalization and physician claims databases, AHS laboratory database, Alberta Kidney Care North and South databases
All-cause mortality	Death from any cause within 1 year after procedure	Alberta vital statistics database
Patient-Reported Outcome Measures		
Generic quality of life	EQ-5D at 2 weeks and 1 year after procedure	APPROACH database
Cardiovascular quality of life	Seattle Angina Questionnaire at 2 weeks and 1 year after procedure	APPROACH database
Economic Outcomes		
Total costs	Total direct health care costs within 1 year after procedure	AH hospitalization, physician claims, and ambulatory care databases
Cost utility	Total direct health care costs per quality adjusted life year	AH hospitalization, physician claims, and ambulatory care databases

AH, Alberta Health; AHS, Alberta Health Services; APPROACH, Alberta Provincial Program for Outcome Assessment in Coronary Heart Disease; CI-AKI, contrast-induced acute kidney injury; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; Contrast RISK, **Contrast** **R**educing **I**njury **S**ustained by **K**idneys; eGFR, estimated glomerular filtration rate; EQ-5D, Euro Quality of Life−5 Dimensions; IV, intravenous.

*Descriptive information on the extent of revascularization will also be reported.

Specific facilitators and mitigation strategies to address each of these assumptions are outlined in more detail in the Supplementary Material.

Rationale for stepped-wedge design

The stepped-wedge design is distinct from traditional 2-arm experimental designs in that all participants will eventually receive the intervention. There are a variety of rationales as to why a stepped-wedge trial is used over a classical randomized control trial.[43] In particular, this study was designed as a stepped-wedge for 2 primary reasons.

First, the stepped-wedge design allows us to provide detailed educational sessions to each of the units in a small group format. These sessions were identified by stakeholders as a critical component of the intervention for motivating sustained behavioural changes. A previous systematic review demonstrated that large group, lecture-style educational sessions are frequently ineffective at improving physician behaviour.[44] In contrast, a small-group format involving

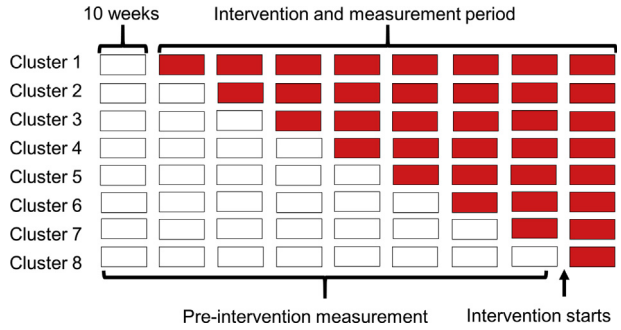

Figure 4. Randomized step wedge design of the trial to reduce contrast-induced injury sustained by kidneys during cardiac catheterization (**Contrast** **R**educing **I**njury **S**ustained by **K**idneys [Contrast RISK]).

different forms of educational media and participant engagement has been shown to be more successful at changing physician practices.[45] The stepped-wedge design allows the research team to provide a sequence of personalized, small-group education to each cluster of physicians just before their introduction to the initiative.

Second, given the evidence that limiting the volume of contrast material delivered and maximizing safe IV fluid administration reduces the risk of developing CI-AKI,[14-21] it is reasonable to assume that this intervention is more likely than not to minimize the rate of development of CI-AKI. Accordingly, a stepped-wedge design will allow all participants eventually to benefit from receiving the intervention, whereas a simple cluster-randomized control trial would deny the control group access to an important quality improvement opportunity, which was deemed undesirable by project stakeholders. The stepped-wedge design will allow all physicians to adopt the intervention for prevention of CI-AKI, while more powerfully ascribing improvements in care and outcomes to the intervention rather than secular trends.

Anticipated challenges

An anticipated risk to perceived or apparent effectiveness of the intervention is that physicians and unit staff may interact with one another, potentially raising awareness of the study and focus on prevention of CI-AKI, leading to contamination of effect from physicians who have been stepped into the intervention to those who have not. However, this effect is expected to be minimal in comparison to the effect of the intervention because it is less likely that these physicians will be able to tailor behavioural changes to patient risk with similar fidelity without the decision support information provided at the point of care. To assess whether contamination is present, we will examine temporal changes in the process and outcome measures of patients before the start of the study and for patients cared for by physicians before they are stepped into the intervention group to determine if measures improve in the preintervention group over time, which will indicate contamination. Should an effect on patient care and outcomes be observed in the study despite this risk of contamination, it is likely to be a conservative estimate of the effect of the intervention.

Ethics approval

The Contrast RISK initiative was granted a waiver of patient consent from research ethics boards at the University of Alberta and University of Calgary, as justified by the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans. The rationale includes that no aspect of the project will introduce additional risk beyond what is present in the current standard of care because the intervention is primarily targeted at improving existing cardiac catheterization laboratory practices. Although patients will sacrifice a degree of autonomy because they are not offered the opportunity to consent to participate, the nature of the intervention prevents patients from being able to opt in or out of the intervention meaningfully, regardless. By consenting to cardiac catheterization procedures, patients will be treated in laboratories that are participating in a system-wide quality improvement initiative to support uptake of evidence-based treatment approaches. Patient privacy will not be jeopardized, as all clinical collected data are already captured and stored in existing health care databases, and both patients and physicians have the option to consent or decline to participate in additional surveys and interviews to provide information.

Physician consent to participate in data collection for the study can be obtained at the time of the initial educational session with the site-lead. Signed informed consent will be collected from both physicians and allied health care providers before collection of their surveys on the usability of the tool and work-flow processes and for participation in the audit and feedback process.

Conclusions

This initiative takes advantage of existing information technology systems and infrastructure to translate evidence-based strategies into care through point-of-care decision support tools designed to improve provider behaviour to reduce the incidence CI-AKI in cardiac catheterization laboratories across Alberta. The use of multifaceted strategies to implement and sustain knowledge and ability to leverage of existing clinical informatics system are critical elements to adopting and evaluating this initiative successfully.

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Supplementary Material

To access the supplementary material accompanying this article, visit the online version of the *Canadian Journal of Cardiology* at www.onlinecjc.ca and at https://doi.org/10.1016/j.cjca.2019.06.002.