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Cumulative Ionizing Radiation Exposure During and After Acute Coronary Syndrome

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Abstract
Radiation exposure from diagnostic and therapeutic procedures is a potential source of iatrogenic harm. The long-term exposure related to a specific diagnosis as opposed to generalized exposure or single episode is not well studied. We sought to determine the long-term cumulative radiation exposure following an acute coronary syndrome (ACS). 278 patients with a first ACS were assessed for cardiovascular procedures requiring radiation. Type of procedure and time of occurrence with respect to the initial ACS event were analyzed. Average radiation exposure by procedure was used to determine cumulative dose per patient and was compared by type of ACS and management. Mean age was 58.9, 73% men, and mean follow up 5.94 years (3.02-9.86). Patients presenting with unstable angina and those undergoing PCI as management choice had the highest exposure. The use of radiation in coronary imaging procedures for the diagnosis and management of ACS occurs early in the disease course, is not insignificant in quantity, and varies by presentation and management choice.

***Keywords* — acute coronary syndrome; iatrogenic harm; imaging; radiation.**

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I. Introduction

There is debate as to the better evaluation of patients presenting with acute chest pain whether it be a structural evaluation (i.e. coronary CT) versus the more common stress model used today.

Given a theoretical linear relationship between radiation exposure and increase in lifetime cancer risk (1)(2), the decision as to which modalities to implement in evaluation of chest pain becomes a more multidimensional question.
Under current practices, the National Council on Radiation Protection and Measurements Reported the average yearly exposure of radiation attributable to cardiac imaging has increased more than 17 times over the past 2 decades (3)(4). A detailed understanding of the radiation exposure patients receive in each aspect of care including diagnosis, treatment and follow up in order to better determine the future methods we employ.

Recent studies designed to assess the risk of cancer radiation exposure related to cardiac imaging have varied in scope, population, and outcomes analysis. These include assessment of cardiac imaging for any indication (5), cardiac imaging over a defined three year time period (6), and cardiac imaging during the initial hospital admission for a diagnosis of an acute myocardial infarction (AMI) (7). More recent studies evaluated cumulative radiation exposure in all patients in a cardiology ward in Europe (20) as well as organ specific exposure in newly diagnosed ischemic heart disease patients within 1 year (21). However, ACS is a broad diagnosis and therapeutic options can be variable based on subtype and resources available. The intent of this study is to quantify the cumulative radiation exposure patients receive following a first diagnosis of the acute coronary syndrome based on subtype and modality of treatment. We evaluated patients with a first ACS with at least 3 years of follow up to quantify radiation exposure as a result of acute and long term cardiac care.

II. Methods

A retrospective study was conducted in a single institution using a database containing 2129 patients referred to cardiac rehabilitation for an approved indication between April 2002 and April 2009. Eligible patients were those with a recent and first ACS with follow up to April 2012. Manual chart review of each case was performed by one of three physician reviewers using the electronic medical record. All admission, discharge, primary care, and cardiology documents were

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reviewed. All patients had given written informed consent to participate in the cardiac rehab database as approved by the Institutional Review Board (IRB HUM00060214). Patients were excluded if they had less than 3 years of follow up, age greater than 75, a prior history of ACS, or having a primary care physician or cardiologist not in our health care system or any documented care outside our health care system.

Patients were categorized into one of three types of ACS as diagnosed at discharge: unstable angina (UA), non-ST elevation myocardial infarction (NSTEMI), or ST elevation myocardial infarction (STEMI); and then categorized based on management during the hospitalization: coronary artery bypass graft surgery (CABG), percutaneous coronary intervention (PCI), or medical management (MM). Finally, nine groups referred to as "combined subgroups" were determined first by ACS presentation and then subsequent management type.

Charts were reviewed to confirm diagnosis and classification of ACS, and to identify all nuclear medicine imaging (NMI), procedures using fluoroscopy including coronary angiography alone (CA) or with intervention (CAI), and CT coronary angiography (CTA) performed during the initial admission and throughout the entirety of the follow up period. Time between initial ACS event and exposure was also calculated in months.

Total radiation exposure was calculated using the aforementioned procedures for the entire study population and for the following subgroups: ACS type, management type, and the combined subgroups. Radiation exposure attributable to NMI, CA/CAI, and CTA was obtained from previously published values (10)(11), and total exposure for each individual calculated.

Group demographics were evaluated to determine differences in patient populations by ACS type and management categories. Pearson's Chi-square test was used to determine significant differences between each of the three sub-categories of ACS and management type. Descriptive statistics for radiation exposure including mean, standard deviation, and confidence intervals were calculated for all sub-categories of radiation exposure and for each of the three exposure types. The linear-no-threshold model was used to calculate cancer risk post-exposure (2). ANOVA analysis was performed on the mean radiation exposure for each type, comparing across all three sub-categories within the broader categories of ACS and management type. For statistically significant ANOVA p-values, an independent samples t-test was performed to calculate a p-value between each of the sub-categories of note, determining between which two groups the significance existed. Statistics were performed using IBM SPSS Statistics 20.0.0.1.

III. RESULTS

A. Study Population

Two-hundred and seventy-eight of the 2129 patients referred to cardiac rehabilitation following an ACS met the study criteria. Patient demographics with relative rates of diagnosis and treatment type are shown in Appendix I. Mean age was 58.9 ± 9.17yrs (range 27.8 – 75.6) and 73% percent were male. Patients self-identifying as white composed 89% of the population. Average follow-up was 5.94 ± 1.83 years. STEMI was the most common presenting diagnosis (46%) with UA and NSTEMI having similar occurrence rates (26% and 28% respectively). CABG, PCI, or MM were the management choice in 26%, 64%, and 10% of patients respectively. There was a significant difference in age of presentation greater than or less than 60 between management groups ($p = 0.01$) and between combined groups (0.008) driven by older age for CABG patients; there was no difference in age between ACS groups, and no difference in gender or ethnicity between ACS groups, management groups, or combined groups (Appendix I).

B. Radiation Exposure

The average radiation exposure received from cardiac imaging from date of initial ACS event through up to 10 years of follow up was 30.68mSv ± 19.01mSv. CA and CAI accounted for 15.5% and 44.5% of this total, respectively, while NMI comprised 36.9% and CTA just 3.1%. The distribution of total radiation exposure received for the total population is seen in Figure 1.

Comparing ACS presentation groups there was a trend toward increased radiation in UA compared to NSTEMI and STEMI.

When compared by initial management, there was a statistically significant exposure difference identified between all three groups. There was a significant difference in radiation exposure between CABG population and PCI population, and a trend toward significance between the PCI population and those treated with medical management (MM).

When evaluated by combined group type, a statistically significant difference in total radiation exposure existed between all nine groups; however there was no statistical difference between any two isolated groups. The highest radiation exposure was found in unstable angina/PCI, and the lowest was NSTEMI/medical management (Table I).

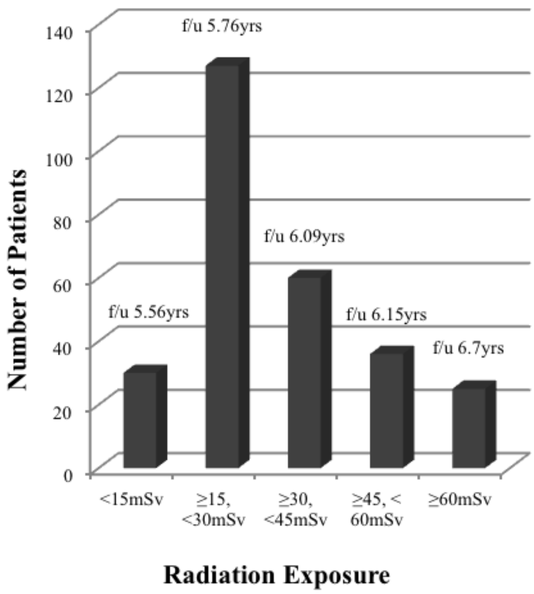

Fig. 1: Cumulative radiation dose from coronary imaging

C. *Timing of Radiation Exposure*

The vast majority of radiation exposure occurred within 3 months of diagnosis of ACS as seen in Figure 2 with 46.5% of all radiation exposure occurring in the first month of diagnosis. This was driven by 61% of all coronary angiography occurred in the first month following diagnosis. Interestingly, only 19.8% of all nuclear imaging and CTA occurred in that first month.

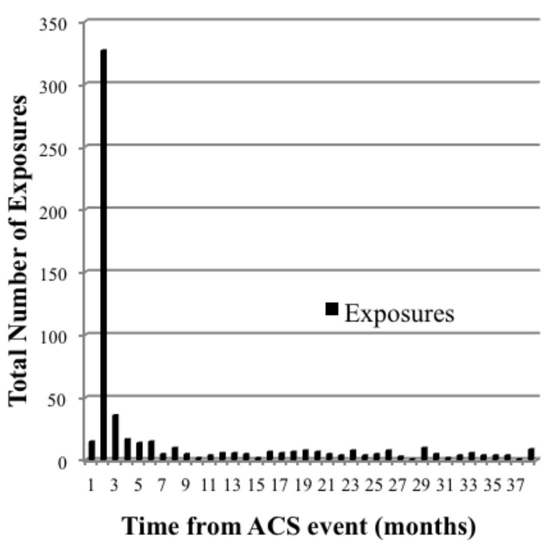

Fig. 2: Time from ACS event until coronay imaging radiation exposure

IV. DISCUSSION

In our single institution study conducted at an academic medical center, patients had an average 31mSv of radiation exposure during evaluation and management over an average of six months follow-up following an ACS event. This is similar to previously reported data in studies using billing codes to identify exposure during an index hospitalization and at up to three years follow-up (7,12). Overall, no significant differences were found between ACS presentation types and the amount of radiation exposure. When evaluated by management type, PCI had a statistically significant increased radiation exposure when compared to CABG, which likely is explained by the increased radiation exposure occurring with PCI as opposed to diagnostic angiography alone. Nearly half of all radiation exposure occurred within the first month of an ACS event, and 80% of the exposure occurred within the first 36 months.

Radiation Results	**Avg Rad Exp**
All	30.68 ± 19.01
UA	33.25 ± 21.72
NSTEMI	26.95 ± 16.61
STEMI	29.84 ± 15.63
p-Value	0.073
UA vs NSTEMI	0.075
UA vs STEMI	0.631
NSTEMI vs STEMI	1
CABG	26.79 ± 21.55
PCI	33.19 ± 17.78
MM	24.74 ± 17.46
p-Value	***0.012***
CABG vs PCI	***0.046***
CABG vs MM	1
PCI vs MM	0.083
UA/CABG	27.91 ± 23.55
UA/PCI	37.98 ± 19.56
UA/MM	26.49 ± 21.16
NSTEMI/CABG	24.55 ± 15.6
NSTEMI/PCI	29.28 ± 15.91
NSTEMI/MM	21.63 ± 15.1
STEMI/CABG	24.58 ± 13.89
STEMI/PCI	30.65 ± 15.94
STEMI/MM	30 ± 15.75
p-Value	***0.023***
UA/CABG vs UA/PCI	0.158
UA/PCI vs NSTEMI/CABG	0.533
UA/PCI vs NSTEMI/PCI	0.587
UA/PCI vs NSTEMI/MM	0.148
UA/PCI vs STEMI/PCI	0.877
(all others have p = 1.0)	

Table 1: Cumulative radiation exposure from coronary imaging in ACS

Cardiovascular disease remains one of the most prevalent conditions in our population (22). As new modalities are introduced and studied in comparison to current management for acute coronary syndrome and subsequent ischemic cardiac disease, consideration of the amount of radiation exposure patients undergo is of significant importance, especially in younger populations. This is the first study from a non-single payer system to look into cumulative radiation exposure over an average of 6 years following initial diagnosis of ACS. Additionally, this is the first study to subgroup the population based on ACS type and modality of management. It is also notable that our study is different from most in that ICD coding was cross-referenced by meticulous chart review to confirm diagnosis and imaging purposes.

Our study was not without limitations. First, nationally accepted values for radiation exposure per procedure were used. A study could attempt to use true radiation exposure for each procedure and for each patient however this is inordinately difficult given tremendous variance in patients and facilities. Previous studies with a similar scope as our own have also relied on standard averages that are well accepted, adding to external validity and generalizability (7)(19). Our study also looked strictly at coronary imaging. Patients with ACS are often exposed to radiation from non-coronary specific CT imaging and/or subsequent electrophysiology procedures, which we did not investigate. Our study was also based on one single academic center, which limits generalizability. Finally, the population meeting inclusion criteria was small, and the study potentially underpowered to elucidate all significant differences in exposure.

Future investigation including longitudinal prospective studies evaluating for radiation exposure and actual cancer incidence would provide further understanding of the true risk ACS patients undergo from imaging procedures. This is particularly important given the potential for iatrogenic harm from radiation use in young cardiac patients and in a large outlier population receiving high radiation exposure. Our study provides an important foundation on which to build. Future research could directly evaluate cardiac outcomes using radiation imaging correlating with the increased risk of cancer, potentially affecting future practice.

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APPENDIX

Demographics								
	Avg Age	Avg F/U		Age (< 60/60 +)	Gender (M/F)	Ethnicity (W/NW)	Tobacco (Y/N)	DM (Y/N)
Total	58.9 ± 9.17	5.94 ± 1.83		150/128	204/74	247/31	149/129	72/206
UA	60.3 ± 8.51	6.24 ± 1.74		61/68	89/40	113/16	70/59	39/90
NSTEMI	58.6 ± 10.5	5.63 ± 1.92		40/31	49/22	63/8	40/31	17/54
STEMI	56.8 ± 8.62	5.74 ± 1.84		49/29	66/12	71/7	39/39	16/62
			p-Value	0.085	0.3	0.749	0.725	0.275
CABG	62.1 ± 8.48	5.04 ± 13.3		28/44	58/14	63/9	47/25	24/48
PCI	57.9 ± 9.09	5.74 ± 1.75		104/74	126/52	160/18	88/90	39/139
MM	56.8 ± 9.68	5.53 ± 1.78		18/10	20/8	24/4	14/14	9/19
			p-Value	0.010	0.277	0.739	0.69	0.128
UA/CABG	63.8 ± 7.94	6.81 ± 1.74		14/34	39/9	41/7	29/19	14/34
UA/PCI	58.5 ± 8.18	5.85 ± 1.65		38/32	43/27	63/7	36/34	19/51
UA/MM	56.3 ± 8.42	6.22 ± 1.72		9/2	7/4	9/2	5/6	6/5
NSTEMI/CABG	59.2 ± 10.8	6.62 ± 2.25		8/6	10/4	14/0	10/4	6/8
NSTEMI/PCI	59.2 ± 10.1	5.4 ± 1.77		24/20	30/14	38/6	23/21	9/35
NSTEMI/MM	55.8 ± 11.9	5.33 ± 1.87		8/5	9/4	11/2	7/6	2/11
STEMI/CABG	58.1 ± 5.09	5.56 ± 1.97		6/4	9/1	8/2	8/2	4/6
STEMI/PCI	56.3 ± 9.21	5.86 ± 1.84		42/22	53/11	59/5	29/35	11/53
STEMI/MM	61.3 ± 3.62	4.3 ± 0.95		1/3	4/0	4/0	2/2	1/3
			p-Value	0.008	0.90	0.704	0.460	0.146

Table A: Baseline Patient Demographics