"INCIDENCE OF CONTRAST INDUCED NEPHROPATHY FOLLOWING CONTRAST ENHANCED COMPUTED TOMOGRAPHY"

By

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Under the Guidance of

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I hereby declare that this dissertation entitled **"INCIDENCE OF CONTRAST INDUCED NEPHROPATHY FOLLOWING CONTRAST ENHANCED COMPUTED TOMOGRAPHY"** is a bonafide and genuine research work carried out by me under the guidance of **Dr. N.RACHEGOWDA**, Professor & Head, Department of Radiodiagnosis, Sri Devaraj Urs Medical College, Kolar, in partial fulfilment of University regulation for the award "**M. D. DEGREE IN RADIODIAGNOSIS**", the examination to be held in April 2019 by SDUAHER. This has not been submitted by me previously for the award of any degree or diploma from the university or any other university.

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Dr. NISHI KANT

LIST OF ABBREVIATIONS

AKI - Acute kidney injury

BMI - Body mass index

CECT - Contrast enhanced computed tomography

CIN - Contrast induced nephropathy

CM - Contrast media

CTA - Computed tomography angiography

CT - Computed tomography

DM - Diabetes mellitus

ED - Emergency department

GFR - Glomerular filtration rate

HOCM- High osmolar contrast media

HTN- Hypertension

ICU - Intensive care unit

IOCM - Iso osmolar contrast media

IV - Intra venous

KUB - Kidney, ureter and bladder

LOCM - Low osmolar contrast media

PE - Pulmonary embolism

PA- Pulmonary angiography

R = recovered

Sr.Cr- Serum creatinine

SD- Standard deviation

ABSTRACT

Background: Contrast induced nephropathy is a major adverse event following use of non-ionic iodinated contrast medium. The incidence of CIN in rural population is not known. It is important to assess the incidence of CIN and to evaluate common risk factors, which may predispose to CIN.

Aims and Objectives: To determine the incidence of contrast induced nephropathy following use of non-ionic contrast in contrast enhanced tomographic studies and to evaluate the risk factors that can predispose development of contrast induced nephropathy

Methodology: This observational study was conducted for a period of 18 months from January 2017 to June 2018 in a total of 310 patients who underwent contrast enhanced computed tomography examination with non-ionic contrast.

Results: The mean age of patients in our study was 52.6 years ± 16.4 years (mean ± SD) (range 23 to 90 years). There was a slight male preponderance (n = 174; 56.1%). CIN was observed in 12 patients (3.87%) all of whom had at least one risk factor. CIN resolved in all patients by seven days without any complications. The commonest contrast examination performed in our study was CECT abdomen in 111 patients (35.8%) followed by CECT neck (n = 80; 25.8%). The mean serum initial serum creatinine level was 1.135 ± 0.163 mg/dL (mean ± SD) (range 0.8 to 1.5 mg/dL). The risk factors evaluated in our study were elderly (n = 67; 21.6%),

hypertension (n = 30; 9.7%), diabetes mellitus (n = 26; 8.4%), NSAID use (n = 10; 3.2%) and renal insufficiency (n = 3; 1.3%). Risk factors were seen in 102 patients (32.9%). Among them, 72 patients (23.2%) had one risk factor followed by two risk factors in 25 patients (16.13%) and lastly five patients (4.84%) had three risk factors with total of 137 risk factors. Risk factors were hypertension in five patients (1.61%), diabetes mellitus and elderly age group in four patients each (1.29%), renal insufficiency in two patients (0.65%). None of the patients with history of NSAID use developed CIN.

Conclusion: We observed a modest risk of CIN following CECT studies. The risk factors for developing CIN were diabetes mellitus, elderly age (>65 years), hypertension and renal insufficiency. Serum creatinine levels reached baseline in all the patients who developed CIN within a week. We concluded that use of non-ionized iodinated contrast media is associated with low risk of CIN and that CECT studies do not cause significant increase in CIN.

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INTRODUCTION

Contrast media have increasingly been employed in most of the computed tomographic (CT) studies. Current CT imaging is largely dependent on contrast enhanced CT (CECT) studies. With the increase in use of contrast media there has been an increase in contrast media-related adverse events. Contrast induced nephropathy (CIN) is considered as a major adverse event following intravenous iodinated contrast use. The most commonly used definition of CIN is an absolute (≥ 0.5 mg/dL) or relative (≥25%) rise in serum creatinine from baseline within 48 to 72 hours. CIN has been considered as third commonest cause for hospital acquired renal failure with an incidence as high as 11% following impaired renal perfusion and nephrotoxic medications, thus highlighting its seriousness[1,2].

CIN has also been associated with increased morbidity and mortality[3,4]. CIN has also been shown to increase hospital stay and increase risk of cardiovascular diseases ranging from coronary disease to stroke[1].

The overall incidence of CIN in the general population is not known and is known to range from 0.6% to 4.96% from various studies[2,5,6]. The data on CIN in patients who underwent intravenous contrast agents are largely based on intra-arterial cardiac interventions in which high volume and sometime high osmolar contrast iodinated contrast media are employed. This differs to the patient population who undergo CECT studies as high amount of contrast and high osmolar contrast media are not employed. These factors may play role in development of CIN[5]. There is a

lacuna between evidence-based guidelines and daily practice of radiologists for CIN prevention. It is therefore essential to estimate the prevalence of CIN in patients undergoing CECT studies and to identify the population who are at risk of CIN[6]. Comorbidities such as diabetes mellitus, advancing age, hypertension, use of non-steroidal anti-inflammatory drugs (NSAIDs) and renal insufficiency are known to increase risk of CIN[5].

There is paucity of data on risk of CIN in patients undergoing CECT studies in our population. Furthermore the risk factors for CIN in our population also need to be identified. Therefore this study has been undertaken to estimate the incidence of CIN in patients undergoing CECT and to identify risk factors that predispose CIN in rural population.

AIMS AND OBJECTIVES

The objectives of the study are:

1. To determine the incidence of contrast induced nephropathy following use of non-ionic contrast used in contrast enhanced computed tomographic studies.

2. To identify the risk factors that can predispose development of contrast induced nephropathy.

REVIEW OF LITERATURE

ANATOMY OF URINARY TRACT

Kidneys

The kidneys are associated with excretion of water and metabolic waste products, thus playing an important role in maintaining water and electrolyte balance[7,8]. Apart from this the kidneys also have endocrine functions such as production and release of erythropoietin (involved in red blood cell formation), renin (blood pressure control) and 1,25-di-hydroxycholecalciferol (active form of vitamin D involved in calcium metabolism), etc[7].

The kidneys are located posteriorly behind the peritoneum on each side of the vertebral column and are surrounded by adipose tissue (Figure 1). "The right kidney is generally situated slightly inferior to the left, due to its relationship to the liver, which is situated superiorly. The left is a little longer and narrower than the right and lies nearer the median plane. The long axis of each kidney is directed anterolaterally and the transverse axis posteromedially" (Figure 2, Figure 3)[7].

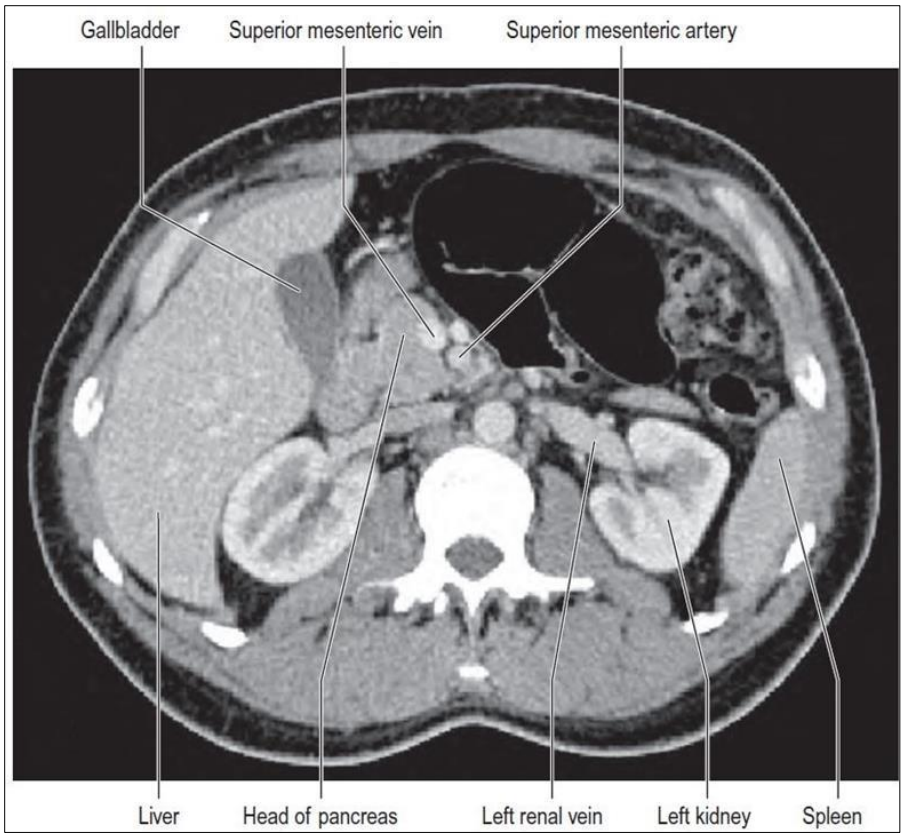

Figure 1. Axial contrast enhanced CT of the kidneys showing anatomical relationships of the kidneys at the renal hilum.

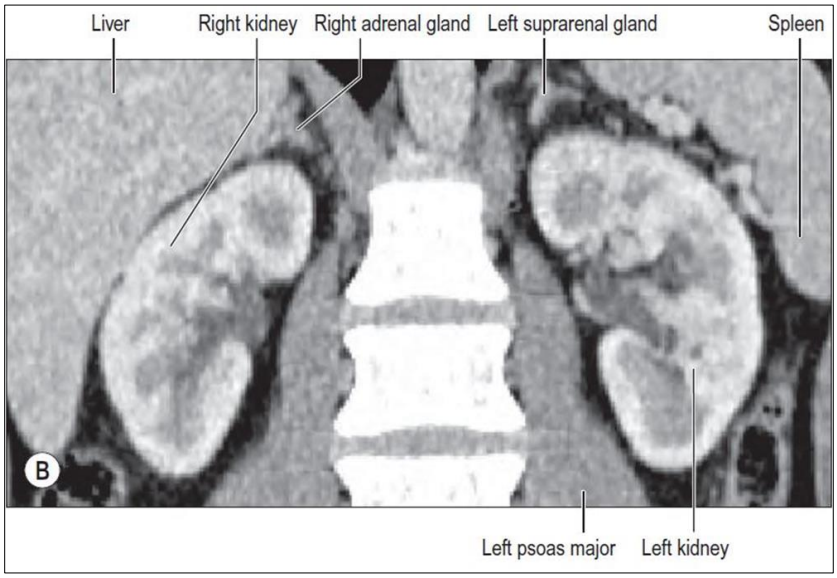

Figure 2. Coronal reformat of contrast enhanced CT showing both kidneys and the suprarenal glands.

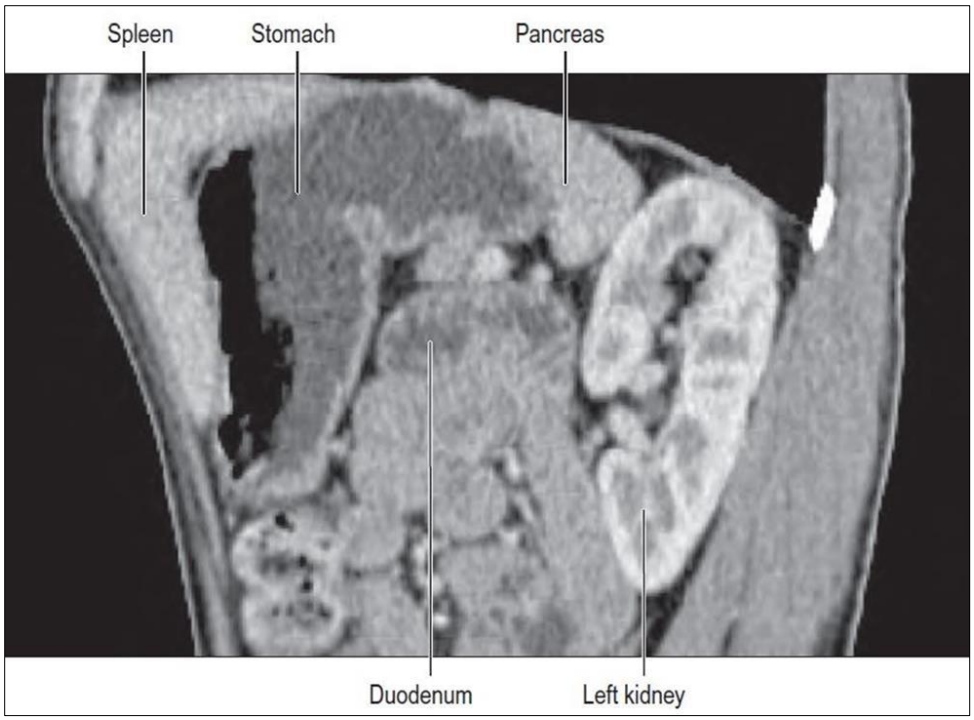

Figure 3. Sagittal reformat of contrast enhanced CT of the left kidney lying posterior to the stomach, spleen and pancreas.

Each kidney typically measures approximately 11 to 12 cm in length, 6 cm in breadth and 2.5 to 3 cm in anteroposterior (AP) dimension. The left kidney may be about 1.5 cm longer than the right; however, it is rare for the right kidney to be greater than one cm long compared with the left. The average weight of kidneys is ~125-170 g in men and 115-155 g in women[7,9]. It is subdivided into 8–10 lobes, each of which is composed of around one cm thick overlying cortex and a renal pyramid, the apex of which (papilla) opens into a minor calyx (Figure 4)[9].

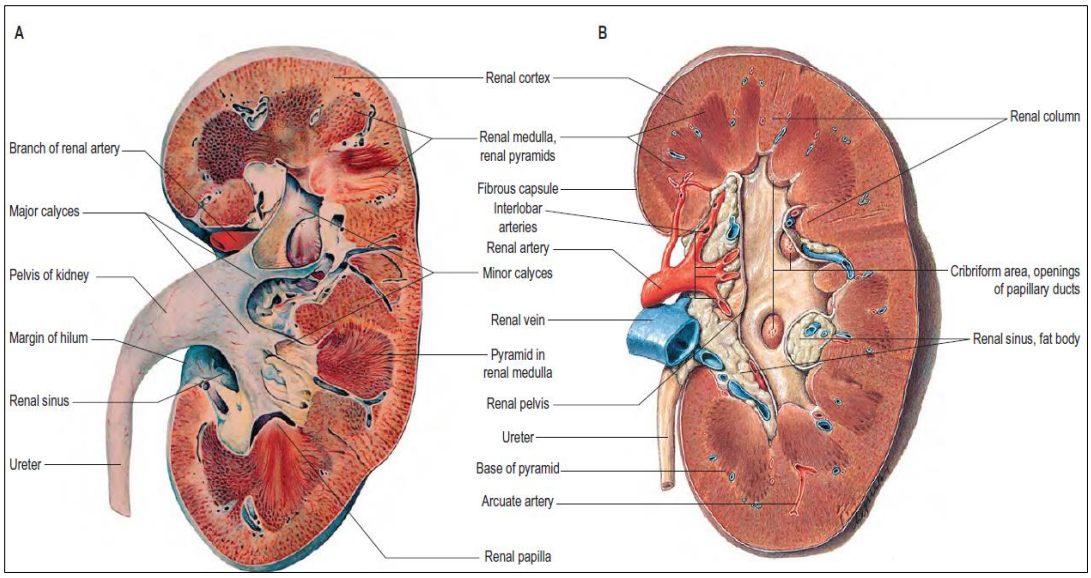

Figure 4. Left kidney, oblique vertical hemisection showing normal macroscopic appearance of the renal cortex and renal medulla and the major structures at the hilum of the kidney. (Left) the fat body of the renal sinus and most of the major vessels at the hilum have been removed, and the renal pelvis has not been opened. (Right), the renal pelvis has been opened to reveal the interlobar arteries.

The kidneys are surrounded by a fibrous capsule which demarcates it from surrounding perirenal fat. The cortex forms the outer part of the renal parenchyma surrounding the medulla, which is made up of the renal pyramids arranged around the renal sinus. The septa (columns) of Bertin are projections of renal cortex in between the pyramids that extend to renal sinus[10].

The collecting system, major arteries and veins form renal sinus, all of which are enclosed by renal sinus fat. The pyramids project into calyces of collecting system, which finally coalesce forming renal pelvis. Although, renal sinus opens on medial part of the kidney; majority of renal pelvis is situated within the renal sinus.

Sometimes it may project outside the kidney to variable extent, resulting in extrarenal pelvis[10].

Renal Pelvis and Calyces

The hilum of the kidney leads to central renal sinus, which is lined by the renal capsule and occupied by renal pelvis, vessels, and fat. The collecting tubules of nephrons drain into the renal papillae in the renal sinus, which finally drain into minor calyces (funnel-shaped expansions of the upper urinary tract). External surface of kidney is encased by renal capsule that continues through the hilum and lines renal sinus, and ultimately fuses with adventitial coverings of minor calyces. Minor calyces surround either a single papilla and may rarely have two or three papillae. The minor calyces unite to form two or possibly three larger chambers, referred to as major calyces[7].

There is considerable variation in the arrangement of the calyces. The calyces ultimately drain into the infundibula, which forms the renal pelvis. A wide variation in arrangement of the infundibula has been observed. The funnel-shaped renal pelvis tapers as it passes inferomedially, traversing the renal hilum and continues as ureter (Figure 4).

The calyces, renal pelvis and ureter can be well visualized radiologically following an intravenous urography (IVU) or CT urography study; or after performing ascending pyelography (cystourethrography). Normal cupping of the minor calyces by projecting renal papillae may be obliterated by conditions that cause

hydronephrosis, chronic distension of the ureter and renal pelvis due to upper or lower urinary tract obstruction resulting in elevated intrapelvic pressure[8].

Ureters

The ureters are two muscular tubes measuring 25–30 cm in length which transfer urine from kidneys to urinary bladder via peristaltic contractions. Ureters are thick-walled and narrow and continuous superiorly with renal pelvis. Ureters descend slightly medially, anterior to psoas major, and enter the pelvic cavity where they the initially curve laterally, then medially, to open into the base of the urinary bladder. The is about 3 mm in diameter, but can be slightly less at its junction with the renal pelvis, at the brim of the lesser pelvis near the medial border of the psoas major muscle, and where it runs within the wall of urinary bladder, which is its narrowest part[7].

The distal 1–2 cm of each ureter is enclosed within an incomplete collar of non-striated muscle, which forms a sheath (of Waldeyer). The ureters pierce the posterior aspect of the bladder and run obliquely through its wall for a distance of 1.5–2.0 cm before terminating at the ureteric orifices. This arrangement is believed to assist in the prevention of urinary reflux into ureter, as intramural ureters are believed to be occluded during increased bladder pressure and during micturition. In the distended bladder, in both sexes, the ureteric openings are usually 5 cm apart and 2.5 cm apart when the bladder is empty[7].

Urinary Bladder

The urinary bladder is an expansile reservoir to hold urine and hence its size, shape, position and relations all vary according to its content and the state of neighboring viscera. When the bladder is empty, it lies entirely in the lesser pelvis, but as it distends it expands anterosuperiorly into the abdominal cavity. An empty bladder is likened to tetrahedral shape and has a base (fundus), neck, apex, a superior and two inferolateral surfaces[11].

Renal microstructure

"The kidney comprises of multiple tortuous, densely packed urinifrous tubules, surrounded by connective tissue consisting of blood vessels, lymphatics and nerves. Each tubule is made up of two embryological distinct parts, the secreting nephron and collecting tubule"[7].

"The nephron comprises a renal glomerulus, which causes filtration from the plasma, and a renal tubule, causing selective resorption from the glomerular filtrate to form the urine. Collecting tubules carries urine from several renal tubules and transports to a terminal papillary duct, opening into a minor calyx at the apex of a renal papilla"[7].

Renal corpuscle

"Renal corpuscles are small rounded structures averaging about 0.2 mm in diameter present in the renal cortex and columns, except in a narrow peripheral cortical zone. Approximately, 1 - 2 million renal corpuscles are present in each kidney, which reduces in number as age advances. Each consist of central glomerulus of vessels and a membranous glomerular capsule, the commencement of a renal tubule"[7].

Glomerulus

Glomerulus is a collection of convoluted, capillary blood vessels, united by scant connective tissue. It is supplied by an afferent arteriole which enters the capsule and an efferent arteriole, which emerges from the vascular pole of the capsule. Glomeruli are simple in form until late prenatal life; few of them remain in simple form for about 6 months after birth, the majority maturing by 6 years and all by 12 years of life[7].

Glomerular capsule (of Bowman)

Bowman's capsule is an expanded blind end of renal tubule, which is deeply invaginated by glomerulus. The outer wall is lined by simple squamous epithelium. The glomerular, juxtacapillary wall is composed of specialized epithelial podocytes. Between these two walls there is a flattened urinary space, called as Bowman's space. This space is continuous with proximal convoluted tubule. Podocytes refer to stellate cells, whose primary foot processes curve around capillary loops and branch into secondary processes, which are in closely applied to basal lamina. Terminal pedicels

are formed by the secondary and tertiary processes. The pedicels interdigitate tightly separated with a narrow gap (~ 25 nm), through filtration occurs[7].

The glomerular endothelium is finely fenestrated. Glomerular basal lamina, fused endothelial and podocyte basal laminae form the principal barrier for passage of fluid from capillary lumen to urinary space. This selective filter is approximately 0.33 μm thick and allows for passage for water and various small molecules and ions from blood under pressure under pressure. Although hemoglobin may sometimes pass through this filter, larger molecules and those with negative charge are usually retained. Protein molecules, which pass the filter are usually reabsorbed and degraded[7].

Renal/Uriniferous tubule

This consists of glomerular capsule, which leads into proximal convoluted tubule (PCT). PCT is connected to capsule from short neck. The renal/uriniferous tubule continues into sinuous or coiled convoluted part. As it near medulla, it straightens and continues as descending thick limb of Henle, U turn and finally ascending limb of Henle, which continues into distal tubule (Figure 5) [7].

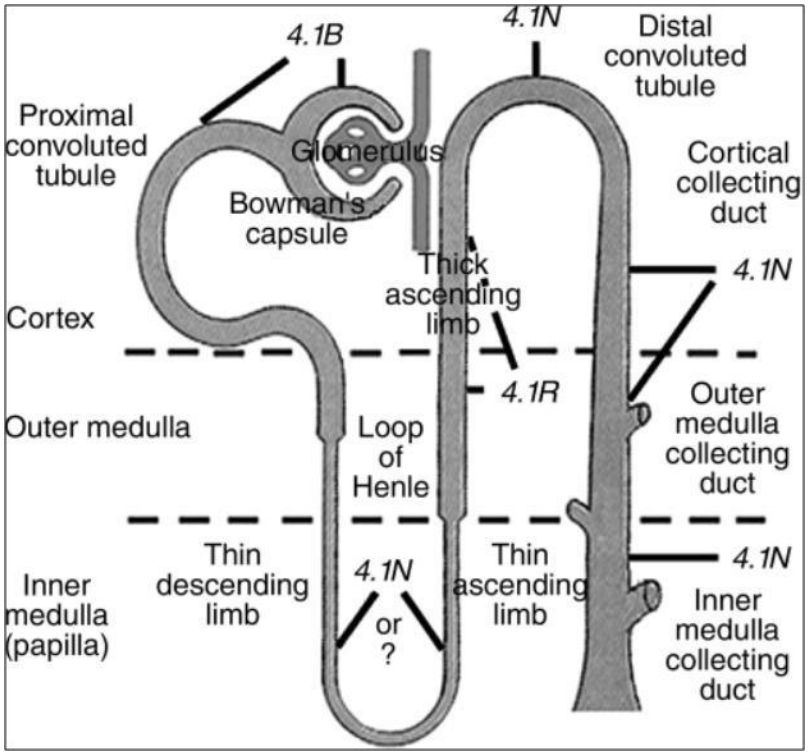

Figure 5. Renal microstructure.

PHYSIOLOGY OF URINE PRODUCTION

Urine production is primary function of kidneys, which are achieved through three steps, which include:

1. Glomerular filtration

2. Selective reabsorption

3. Concentration of urine

Glomerular filtration

This involves passage of water containing dissolved small molecules from blood plasma to the urinary space in the glomerular capsule. Due to the selective permeability of the glomerular basal lamina, larger molecules such as plasma proteins (>70 kilo Dalton) and those with net negative charge, polysaccharides, lipids and cells, are usually retained in blood. Filtration occurs along the pressure gradient existing between the larger glomerular capillaries and urinary space. These are separated by glomerular basal lamina. It is important to note that this gradient exceeds osmotic pressure of blood. There is arteriolar pressure gradient between afferent and efferent glomerular arterioles as afferent glomerular arteries are wider than efferent glomerular arterioles, thus creating pressure gradient. The rate of filtration can therefore be altered by modifying the tone of the glomerular arterioles. Initially, the glomerular filtrate is isotonic with glomerular blood[7].

The assessment of glomerular filtration is essential in diagnosis and management of renal glomerular pathology as clearance depends on the glomerular filtration. Similarly glomerular filtration is important in chronic kidney disease as it helps in timely management. Glomerular filtration rate (GFR) is calculated based on the renal clearance of a marker in plasma, which is expressed as the volume of plasma completely cleared of the marker per unit time. GFR markers may be endogenous (creatinine, urea) or exogenous (inulin, iothalamate) substances. The ideal marker should be endogenous, freely filtered by the glomerulus, neither reabsorbed nor secreted by the renal tubule, and eliminated only by the kidney[7].

Selective resorption

Selective resorption from the filtrate is an active process which occurs predominantly in the proximal convoluted tubules. In this process, smaller molecules such as glucose, phosphate, chloride, amino acids, calcium, sodium, and bicarbonate, and small proteins (e.g. albumin) get reabsorbed through endocytosis. As proximal tubules are permeable to water, the filtrate is locally isotonic as compared with blood as extra water passes through the tubules freely. The remaining part of tubule reabsorbs most of the water (up to 95%), therefore when urine reaches the calyces it is greatly reduced in volume and is hypertonic to blood. The process relies on the establishment of high osmolality in the medullary interstitium, so as to exert sufficient osmotic pressure in the water-permeable regions of renal tubule. This pressure gradient is achieved through countercurrent multiplier mechanism[7].

Concentration of urine

This filtrate at distal part of convoluted tubule is hypotonic. This is achieved by selective reabsorption of Na^+ and Cl^- ions by ascending limb and distal tubular cells, which are under aldosterone control. Once the filtrate reaches the collecting ducts, the contents re-enter high osmotic pressure region by descending again through the renal medulla. Collecting ducts are lined by cells, which show variable permeability to water based on the neurohypophysial ADH signal. There is movement of water depending on osmotic gradient, which exists with the adjacent extratubular spaces. The tonicity of filtrate gradually increases along the collecting ducts and at the tip of renal pyramids it is higher than that of blood. This mechanism is complex and highly flexible to meet physiological requirements. It is affected by the balance between the rate of filtration and absorption can be varied. Hydrogen and ammonium ion concentration control is critical in regulation of acids and bases in the blood. Ions are secreted at several sites. It has been shown that more than 91% of ingested potassium gets excreted in urine. This process is achieved largely through secretion of potassium by cells lining the distal tubule and collecting duct[7].

IODINATED CONTRAST MEDIA

Contrast media: Definition, History and Development

The European Parliament and Council of European Union have defined medicinal product as "any substance or combination of substances which may be used in or administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or to making a ***medical diagnosis***"[12]. Considering this definition contrast media are considered as medicinal product.

The history of search for contrast media can be traced back to discovery of X-rays, when it was felt that there was a need for better contrast visualization for some organs. The obvious choices were elements with high atomic numbers as they theoretically block X-rays and produce better contrast and therefore bismuth, lead, barium, and iodine salts were considered the obvious choices. Haschek and Lindenthal in Vienna performed the first angiogram of amputed hand just weeks after Roentgen discovered X-rays. They used mixture of cinnabar (toxic mercuric ore), lime and petroleum, all of which were considered toxic. Later Becker demonstrated anatomy of hollow organs by introducing lead acetate in gastrointestinal tract (GIT) of guinea pig. Since lead is highly toxic, its clinical use was never considered. In the same year Hemmeter at John Hopkins Hospital developed a method of allowing human use of toxic materials. He devised a rubber bag filled with mercury or lead acetate, which the patient would swallow prior to performing the X-ray. Later he replaced this technique with use of bismuth subnitrate, an inexpensive heavy salt,

which was commonly used for peptic disorders. No wonder bismuth salts became popular quickly. However, they eventually got replaced by barium, partly due to side effects of bismuth and partly due to non-availability of bismuth during World War 1. Since then barium have undisputedly been the choice for X-ray studies involving GIT[13].

Parallel to development of contrast agents for GIT, Wittek performed the first cystogram in 1903. He filled urinary bladder with air to outline a calculus. In the same year Wulff injected bismuth subnitrate and starch into urinary bladder lumen and demonstrated what could probably have been a diverticulum. Two years later, Voelcker and von Lichtenberg incidentally imaged upper urinary tract when performing urograms using colloidal silver. They subsequently successfully performed the first successful retrograde pyelogram when they demonstrated renal pelvis by injecting contrast directly into the ureteral catheters. Thus silver compounds were used for imaging of urinary tract. Silver often produced adverse events, some of which were severe and search was made for alternative agents. Although Burns in 1915 used thorium nitrate, it was abandoned later due to its toxic effects. By 1917 Cameron successfully used sodium and potassium iodides and within an year sodium bromide was also introduced[13].

Iodine was already being used during the early 20th century for treatment of syphilis. The initial use of iodinated contrast agents can be attributed to Cameron, who introduced iodine as a contrast agent. He performed cystograms and pyelograms initially on animals and later in humans. By 1923, Osborne and colleagues from Mayo

Clinic performed the first intravenous (i.v.) study using iodine-based compound. The initial iodine compounds intended for i.v. use were considered toxic. Efforts were made to reduce their toxicity, which was led by Binz and Rath from the Chemical Institute of Agriculture College in Berlin. They developed N-methyl-5-iodo-2 pyridone (Selectan-neutral), which was less toxic than iodide salts as the iodine was attached to pyridine ring and therefore there were no free iodide ions. Swick in 1929 modified Selectan-neutral and developed Sodium 2-Oxo-5-Iodo-Pyridine-N-Acetate (Uroselectan). This agent had greater water solubility and iodine content and was less toxic. This set the stage for further developments and soon iodine based contrast agents were widely used in imaging of urinary tract, angiography and myelography[13].

Although iodine based contrast agents had significantly lower toxicity as compared to their previous counterparts, many patients complained of significant pain following i.v. study. It was Torsten Almén who first proposed that pain could be related to hyperosmolarity of contrast media. He proposed that there was a need for development of contrast agent of lower osmolarity, which at that time was considered to be not feasible. It was believed that for any contrast to be soluble in plasma it had to be ionic. Almén with Holtermann and others at Nyegaard & Co finally developed the first nonionic contrast medium in 1968 and was followed by metrizamide, the first commercially available nonionic contrast media. Metrizamide had the advantage of being painless. This broke the mold and paved the way for further refinements resulting in present non-ionic contrast agents[13].

Currently, iodine is the only element that has been proved to be safe and satisfactory for i.v. use in radiography and angiography. Iodine is the only component in the contrast media, which provides opacification; the rest of the materials act as safe carrier for iodine in the blood stream by reducing toxicity and increasing solubility in the plasma. A challenge in developing iodinated contrast has always been safe delivery of iodine in sensitive organs such as brain or kidneys in quantities enough to produce adequate contrast. In fact in some procedures or studies the contrast may also be introduced into the cerebrospinal fluid[14].

The safe carriers for iodine will in all likelihood be organic carriers in the near future. There have been four chemical types of iodinated contrast media, all of which contain three atoms of iodine at positions 2, 4, and 6 and have been referred to as monomers. There are few compounds, which contain six atoms of iodine per molecule and are referred to as dimers. The currently used iodinated contrast media are highly hydrophilic with low lipid solubility, low protein, receptor or membrane affinity and low toxicity with a weight of <2000. Iodinated contrast media are classified based on two properties – ionic or non-ionic nature and the osmolality (Figure **6**). Based on these properties the contrast media are sometimes referred to as first generation, second generation and third generation contrast media[14].

Classification of contrast media

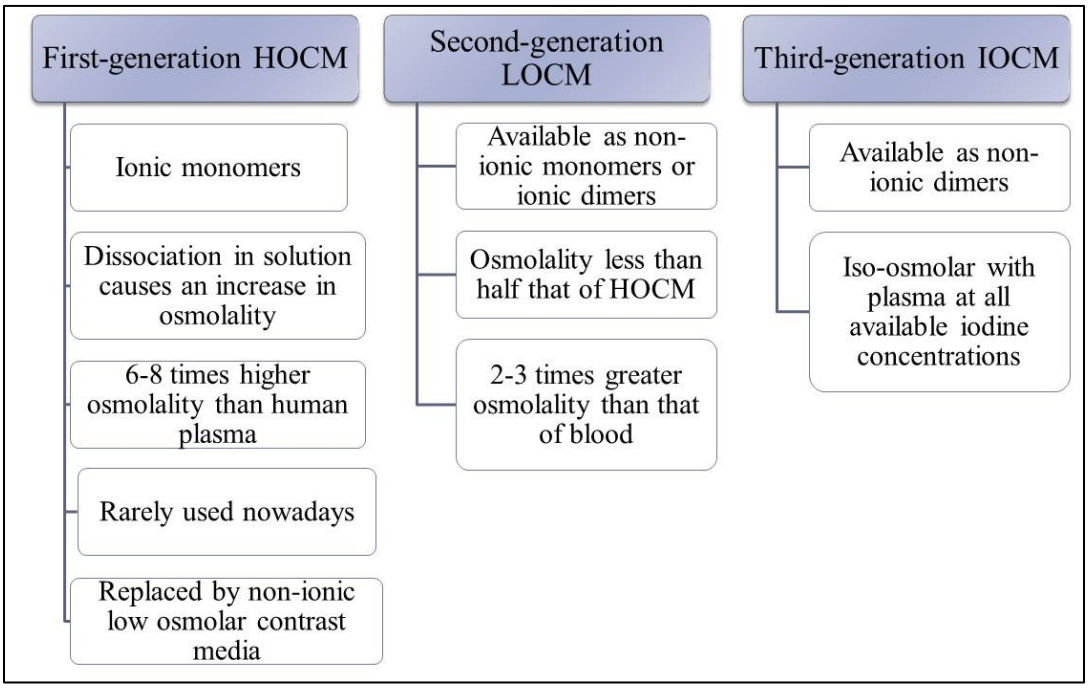

Figure 6. Classification of contrast based on ionic/nonionic nature and osmolality into high osmolar contrast media (HOCM), low osmolar contrast media (LOCM) and iso-osmolar contrast media (IOCM).

Type	Ratio*	Osmolality (mOsm/kg H_2O)	Ionicity	Example(s)
HOCM	3:2	1000-2000+	Ionic	HYPAQUE (diatrizoate) CONRAY (iothalamate)
LOCM	3:1	300+ - 800	Nonionic	OMNIPAQUE (iohexol) IMAGOPAQUE (iopentol) IOPAMIRO/SOLUTRAST/NIOPAM/ ISOVUE (iopamidol) ULTRAVIST (iopromide) OPTIRAY (ioversol) IOMERON (iomeprol) XENETIX (iobitridol)
LOCM	6:2	600	Ionic	HEXABRIX (ioaglate)
IOCM	6:1	290	Nonionic	VISIPAQUE (iodixanol) ISOVIST (iotrolan)

Figure 7. Classification of contrast media with iodine-to-particle ratio, osmolality, iconicity and commercially available compounds in each class.

First generation or High-osmolar ionic iodinated contrast media (HOCM)

All the iodinated ionic contrast media contain either sodium or meglumine (N-methylglucamine) components are the non-radiopaque cation. The radiopaque anion is composed of tri-iodinated fully substituted benzoic acid ring. The commonly used anions are diatrizoate, ioxitalamate and iothalamate. These compounds dissociate completely in water to form anion (tri-iodinate radiopaque component) and cation (non-radiopaque component) with a iodine-to-particle ratio of 3:2 i.e., there are three atoms of iodine for every two particles (anion and cation). As the name suggests, there contrast media are highly hypertonic with an osmolality of up to 1600 mosmol/kg water at iodine concentration of 300 mgI/mL of solution when compared with osmolality of plasma of 300 mosmol/kg water. Due to high osmolality these agents are known for their adverse events. The hyperosmolar compounds are known to cause osmotic effect in surrounding tissues resulting in fluid redistribution (vascular overload). The possible effects of osmotic effect are decompensation in cardiac patients, deformed and rigid red blood cells (RBCs) caused due to cell shrinkage and rarely thrombosis or ischemic events (especially in brain and myocardium). It is due to these adverse events that these compounds are almost abandoned for i.v. use[14].

Second generation or Low-osmolar ionic and non-ionic iodinated contrast media (LOCM)

The adverse event profile of HOCM necessitated the development of contrast media with lower osmolality, which were referred to as low-osmolar ionic contrast

media. There are two types of low-osmolar iodinated contrast media, ionic and non-ionic. Ioxaglate is the only ionic iodinated contrast media, which is mixture of sodium and meglumine salts of monoacidic double benzene ring. The benzene ring has three iodine atoms at C2, C4 and C6 position. Therefore, each molecule of ioxaglate has six iodine atoms (three in each benzene ring) and dissociates into two particles in plasma/ water with a iodine-to-particle ratio of 6:2. The osmolality of ioxaglate is similar to that of other non-ionic contrast media, which are monomers[14].

Low-osmolar non-ionic contrast media are currently the most commonly used contrast media. These are monomers and do not dissociate in water / plasma. The first non-ionic contrast was metrizamide, which was introducted in 1969 by Torsten Almén in 1969 as discussed before. The current non-ionic contrast media are second generation compounds, which include iomeron, iohexol, iopentol, iopamidol, iopromide, ioxilan, ioversol, and iobitridol (Figure 7). These compounds are stable and have very low toxicity making them popular in everyday radiological practice. As these molecules are iodinated non-ionic monomers, they provide iodine to particle ratio of 3:1 (each benzene ring having three atoms/ per molecule of compound). The osmolality of these compounds is about 50% or more lower (~ 600 mosmol/kg water of a 300 mgI/mL solution) than that of high osmolality contrast media[14]. The name low osmolar contrast media is somewhat misleading in that the osmolality is low when compared with high osmolar contrast and not lower than plasma[14].

Iso-osmolar non-ionic contrast media

Even with the development of low osmolar contrast media, there were efforts to develop a contrast media, which has the osmolality close to that of plasma. This led to development of iso-osmolar non-ionic contrast media. These molecules are dimers i.e., they have two benzene rings (six atoms of iodine) and do not dissociate in solution and therefore provide the highest iodine-to-contrast ratio (6:1). Some examples of contrast media in this category include iodixanol, iotrolan, and isomenol. These compounds have a osmolality of about 270 to 300 mosmol/ kg water at 300 mgI/mL of solution. Various electrolytes are also introduced (eg. NaCl, calcium salts) to maintain osmolality of the contrast media. The introduction of these contrast media, posed a challenge in terms of high viscosity. A iso-osmolar contrast media has high viscosity. This may make uncomfortable for the patient and sometimes it is challenging to inject contrast media in small i.v. lines as they are highly viscous. One way to reduce viscosity is warm them to body temperature prior to introduction into body[14].

Pharmacokinetics

None of the contrast agents in any of the aforementioned classes have noticeable pharmacological actions, which makes them ideal for diagnostic use. They are therefore not considered as therapeutic drugs. It is important to understand the pharmacokinetics so as to understand their protein binding capacity and excretion. Once the contrast media enter the blood stream, they are distributed into the extravascular extracellular space due to their high capillary permeability, with the

exception of blood brain barrier, which is very tough. Moreover these contrast agents also don't enter the blood cells or tissues, which is desirable as the contrast agents do not enhance the normal tissues / organs. Contrast media have minimal protein binding. Contrast media follow two-compartment kinetics. The primary excretion is through renal excretion via glomerular filtration. In individuals with normal GFR (>60 mL/min/1.73 m2), more than four-fifths is excretion in the first 4 four hours and nearly 98% is excreted at 24 hours. The renal excretion gets markedly delayed in patients with impaired renal function and it can take days to months for contrast to be excreted by the body. The other minor mode of excretion is through the biliary system, which accounts for <1% of total excretion, which may vary in some individuals. It is for this reason that in some individuals the bile is seen as hyperdense following i.v. contrast media use[14].

Oral hydrophilic contrast agents are not absorbed from the GIT and pass unchanged. One of the drawback of using HOCM is that there is risk of water being extracted from the lumen of GIT due to hyperosmolar media in the GI lumen resulting in dehydration[14].

CT IMAGING: BACKGROUND

There has been a significant improvement in the field of medical imaging in both the technologic and clinical areas following the discovery of X-ray in 1895 by Wilhelm Conrad Roentgen, a German Physicist. Innovations in technology are a norm in the Radiology Department, with introduction of new ideas and methods and

refinements in existing techniques happening continuously. One such evolution is the invention of computed tomography (CT)[15].

The first idea of a computed tomography machine was conceived by Sir Godfrey Hounsfield in 1967 and the first patient was scanned for brain cyst in 1971[15].

Sir Godfrey Hounsfield, an electronic engineer working at the Central Research Laboratories of EMI in England commenced work on image reconstruction in 1968.His original apparatus consisted of a collimated isotope source mounted on a lathe bed. The objects examined were phantoms contained within a ten-inch water. The scan took nine days to complete because of the low intensity of the X-ray radiation source, and a further two and half hours to process the reading through a computer. The resulting image though of poor quality proved that the system worked. To provide sufficient intensity the equipment was modified by replacing the isotope with an industrial X-ray tube[15].

A prototype scanner was then developed and installed in Atkinson Morley Hospital in Wimbledon, England on 1st October 1971. The first patient scan was a 41 year old female with suspected frontal lobe tumor, the tumor was clearly demonstrated on the scan[15].

Hounsfield and Ambrose presented their paper on CT to the annual congress of the British Institute of Radiology on 20th April 1972 to great

acclaim. The first CT papers, by these authors appeared in British Journal of Radiology in 1973. The invention of this technique resulted in the award of 1979 Nobel Prize in physiology and medicine to Sir G. N. Hounsfield, Central Research Lab., England (EMI), and A. N. Cormack of Physics Department, Tufts University, Massachusetts, U.S.A. Advanced Technological Developments. Over the last ten years, four different generations of CT scan equipment were produced. The most important improvements have been in the reduction in the single image generation time from five minutes to 2.5 seconds in the third and fourth generations scanners and an increase in spatial resolution and contrast[15]. The introduction of second generation CT scanners further reduced the scan time from about six minutes to about two minutes. Late second generation CT scanners with $\geq$ 20 detectors further reduced scanning time to about $\leq$ 20 seconds. This dramatically improved quality of body scans, which could not be performed previously within a breath hold. The third generation scanners further reduced the scan time to 5 seconds or less, which has now further improved to about 0.33 seconds[16].

Slip Ring Scanners

There was no significant improvement in CT technology following 4^{th} generation CT scanners in late 1980's. The only limitation at that time was interscan delays. Following one 360^0 rotation, the cables connecting rotating components (x-ray tube and detectors) to the rest of the gantry required rotation to be stopped and reversed for next slice, all of which added time of scan. All this changed with application of low-voltage slip rings. Slip rings provide electricity to the rotating components without fixed connections (Figure 8). Slip rings made it possible for

continuous rotation, thereby reducing scan time. This technology also paved the way for introduction of spiral/helical CT scans[16].

"In the mid-1980s, another high speed CT scanner was introduced, which was referred to as the Electron Beam CT (EBCT) scanner used for imaging cardiovascular system. In 1989, Dr. Willi Kalender introduced volume scanning by using spiral / helical CT scanners. In spiral/helical CT Scanners, a thin X-ray beam traces a path around the patient and scans a volume of the tissue. Recently, dual slice spiral /helical CT scanner and multislice CT scanners were introduced which mainly increase the speed and volume of scan". Volume CT scanning has resulted in a wide range of applications such as CT fluoroscopy, CT angiography, 3D Imaging and virtual reality imaging[15].

Figure 8. Slip-ring technology in Siemens Somatom Emotion CT scanner

CONTRAST INDUCED NEPHROPATHY

One of the adverse events associated with use of iodinated contrast media is the deterioration of renal function, which is also referred to as contrast induced nephropathy. CIN is defined as increase in serum creatinine following use of intravenous iodinated contrast media[17]. Various criteria for diagnosis and classification of CIN have been proposed[1,18,19,20]. The simplest and most widely used criteria is "an absolute increase of serum creatinine by ≥ 0.5 mg/dL or 25% relative increase within 48 to 72 hours after administration of iodinated contrast media in the absence of other cause for rise in serum creatinine" [5,19]. The exact mechanism for CIN is not completely understood and it is believed to be caused due to myriad factors that ultimately play a role in deterioration of renal function[21,22,23]. There are four mechanisms, which are considered to contribute to CIN[22,23,24,25,26]:

1. Contrast medium induced vasoconstriction resulting in renal hypoxia (reduced blood flow).

2. Reduced renal blood flow further results in loss of renal autoregulation, which in turn leads to reduced blood flow to outer renal medulla.

3. Generation of reactive oxygen species due to reduced renal blood flow and contrast media toxicity, which exceeds the anti-oxidant reserve. This causes further renal hypoxia.
4. Contrast media in itself can cause direct cytotoxic effect on renal tubules resulting in renal hypoxia.

CLINICAL STUDIES

A multicenter observational study was conducted by Lee al to determine the incidence of CIN in patients undergoing CECT studies in Korea and to evaluate the risk factors for CIN. The study included data from 16 tertiary care hospitals with a sample size of 101487 patients (total CECT studies performed 140838). The observers found that quarter of patients were >70 years followed by hypertension (13.7%), diabetes mellitus (11.9%), heart failure (1.7%) and gout (0.55%). It was observed that in patients with worsening renal function was associated with increased prevalence of risk factors, in which cases preventive measures to reduce risk of CIN were used. The researchers found that CIN was seen in 2.2% of CECT examinations (n = 3103). Risk of CIN increased with reduced eGFR, diabetes mellitus, and congestive heart failure. The authors concluded the although patients undergoing CECT may have risk factors, preventive measures should be used optimally whenever required to improve patient care[6].

A meta-analysis was conducted by Kooiman et al to evaluate the risk of CIN, chronic loss of renal function and the need for renal replacement therapy (RPT) following CECT study. The authors also evaluated the subgroups at risk for CIN. The meta-analysis included 40 studies. It was observed by the authors that pooled incidence of CIN was 6.4% (65% CI: 5.0 to 8.1). There was very low risk of need for RPT in patients with CIN (0.006%; 95% CI: 0.6 to 2.1%). It was furthermore observed that chronic renal disease (OR 2.26; P<.001) or presence of diabetes mellitus (OR 3.10; P<.001) were associated with significantly increase risk of CIN[27].

Moos et al conducted a meta-analysis to analyze the incidence of contrast-induced nephropathy (CIN) and to evaluate the risk factors for CIN in patients undergoing CECT studies with low- or iso-osmolar iodinated contrast media. The review included 42 studies with a combined population of 18790. They observed that 45% of patients had reduced eGFR <60 mL/min, 55.2% of patients were hypertensive followed by diabetes mellitus in 20.2% of patients and lastly 6.5% of patients had congestive heart failure. The overall risk of CIN was found to be 4.96% (95% CI: 3.79 to 6.47). The authors observed statistically significant association between CIN and presence of renal insufficiency (OR 1.73; 95%CI: 1.06 to 2.82), diabetes mellitus (OR 1.87; 95%CI: 1.55 to 2.26), malignancy (OR 1.79 (95%CI: 1.03 to 3.11), advancing age (>65 years) (OR 1.95; 95%CI: 1.02 to 3.70) and use of non-steroidal anti-inflammatory drugs (NSAIDS) (OR 2.32l 95%CI: 1.04 to 5.19). It was also observed that hypertension (P = .13), anaemia (P = .38) and congestive heart failure (P = .40) were not associated with significantly increased risk of CIN. The authors concluded that the overall incidence of CIN in patients undergoing CECT studies was low and the risk factors for CIN included renal insufficiency, malignancy, diabetes mellitus, advancing age and use of NSAIDs[5].

A review of National Cardiovascular Data Registry Cath-PCI registry was performed by Tsai et al to evaluate the incidence, predictors and outcomes of acute kidney injury (AKI) / CIN in individuals undergoing percutaneous coronary interventions. The review included data from 985737 patients over a period of two years. The authors observed that 7.1% patients (n = 69658) developed AKI and 0.3% of patients (n = 3005) needed dialysis. The key risk factors for AKI included presence of “ST-segment elevation myocardial infarction (STEMI) (OR 2.60; 95% CI: 2.53 to

2.67), severe chronic renal disease (OR 3.59; 95% CI: 3.47 to 3.71), and cardiogenic shock (OR 2.92; 95% CI: 2.80 to 3.04)". Additionally it was also observed that mortality rate in patients developing AKI was 9.7% and increased to 34% in patients who required dialysis vs 0.5% in patients who did not develop AKI (*P*<.001). It was found out that AKI (OR: 7.8; 95% CI:7.4 to 8.1, *P* <.001) and dialysis (OR: 21.7; 95% CI: 19.6 to 24.1; *P* <.001) were independent predictors for inhospital mortality. The authors concluded that about 7% of patients undergoing PCI may develop AKI, which is an independent predictor for inhospital mortality and that there is a need to reduce the risk of AKI[4].

Bhatt et al conducted a study in 250 patients in New Delhi to calculate the incidence of CIN with use of i.v. contrast media and to identify risk factors for development of CIN. It was observed that 10% of study population (n = 25) developed CIN of 84% (n = 21) of patients had transient CIN and RFT returned to baseline. One patient developed renal failure and succumbed to same, while one patient died due to unknown cause. The authors reported that presence of pre-existing renal disease, cardiac failure, dehydration, prior use of i.v. contrast medium, volume of contrast all had significant correlation for risk of CIN (*P*<.05). Other risk factors such as previous renal surgery, diabetes mellitus, hypertension, history of nephrotoxic drug use, and contrast characteristics did not result in significantly increased risk for CIN. The authors concluded that CIN is concerning in everyday routine imaging and should be considered as an adverse effect of use of i.v. contrast media[28].

Mitchell et al conducted a prospective, consecutive cohort study in outpatient population to evaluate incidence of CIN and associated morbidity and mortality

following CECT study. The study included 633 patients and CIN was observed in 70 patients (11%). Of the total population 15 patients (2%) with CIN died within 45 day period and seven patients (1%) developed severe renal failure of whom six patients had CIN. Of these six patients, four patients succumbed most probably due to renal failure. The authors concluded that CIN was "associated with increased risk of severe renal failure and death from renal failure"[29].

Hassen et al conducted a study in 536 patients to evaluate the rate of outpatient follow-up and incidence of CIN in patients presenting to emergency department for CECT abdomen and pelvis study. The risk factors evaluated in their study were diabetes mellitus (18%; n = 96), hypertension (26.3%; n = 141), CKD and CHF (0.9%; n = 5). They observed that only 40 patients followed up within one week following discharge and had lab work up. CIN was seen in 9 of 40 patients (22.5%). A total of 71 patients followed up after one week to within one month with lab investigations of which 11 patients (15%) developed CIN with an overall incidence of 15.3% (17 of 111 patients). The authors concluded that outpatient follow-up is poor in emergency setting and the risk factors for CIN were advancing age, diabetes mellitus and hypertension rather than chronic kidney disease[30].

Hinson conducted a single-center retrospective cohort analysis to determine whether use of i.v. contrast in CECT studies was independently associated with risk of AKI and adverse clinical outcomes. The study included a total of 16801 patients over a 5-year period. The patients were grouped into three groups (those who underwent CECT, unenhanced CT and non-CT study). The authors noted that baseline serum creatinine was similar across all the three groups; however there was

higher eGFR in patients in CECT group. The authors noted that the risk of developing AKI was 10.6%, 10.2% and 10.9 across the three groups (CECT, unenhanced CT and non-CT groups respectively). Furthermore it was also observed the risk of developing AKI in patients undergoing CECT was no more than that observed in patients in unenhanced CT study (OR 1.01; 95% CI 0.92 to 1.12) or in patients who did not undergo CT (OR 1.05; 95% CI 0.94 to 1.18). Furthermore the risk of developing chronic kidney disease within six months of study was 2.0%, 4.6% and 3.5% in CECT, unenhanced CT and non-CT groups respectively. Similarly the risk for renal transplantation was 0%, 0.1% and 0.1% respectively for the aforementioned groups. The probably of need for dialysis across the three groups were 0.4%, 0.9% and 0.6% respectively. The authors concluded that use of i.v. iodinated contrast was not associated with significantly increased risk of AKI[31].

Baird et al evaluated if elderly patient population (>70 years) was at risk for CIN following CECT studies and to predict whether patients developing CIN may require renal replacement therapy. The study included 31 patients who underwent CECT studies of which CECT thorax and CECT abdomen were the major investigations (35.5% each). Although increasing baseline serum creatinine levels were identified in patients >85 years, there was no statistically increase in serum creatinine among the patient subsets (70 to 84 years and >85 years). The authors reported that development of CIN requiring dialysis was 0%. The authors concluded that the older the kidney, it tolerated i.v. iodinated contrast also referred to "Baird Hypothesis"[32].

Rashid et al conducted a retrospective chart review of two tertiary intensive care units (ICU) involving 139 patients to determine incidence of CIN in the setting of ICU and evaluate prevalence of associated risk factors. The authors found that 11.5% of patients (n = 16) developed CIN. It was also observed that >70% of patients had ≥ 2 risk factors. The only risk factor to have significant correlation for development of CIN was advancing age (*P* = .04; odds ratio1.041, 95% confidence interval 1.002 to 1.081). Mortality rate was higher in patients with CIN (31%) as compared with patients without CIN (13%); however, this difference did not reach statistical significance (*P* = .068). It was also observed that length of hospital and ICU stay was statistically not significant in patients with and without CIN. The authors concluded that it is not possible to predict risk of CIN in ICU patients and that further studies may be required to assess the same[33].

MATERIALS AND METHODS

Source of data:

This observational study was conducted in individuals who underwent CECT studies at the Department of Radiodiagnosis at R. L. Jalappa Hospital attached to Sri Devaraj Urs Medical College. Individuals who met the inclusion and exclusion criteria were included in the study. The study was conducted over a period of 18 months (Jan 2017 to July 2018). All the patients underwent baseline renal function test prior to CECT study.

Inclusion Criteria:

The inclusion criterion was:

1. Normal renal function (defined as serum creatinine ≤1.4 mg/dL), which is the standard of care at our hospital

Exclusion Criteria:

The exclusion criteria were:

1. Age <18 years
2. Pregnancy
3. Allergy to contrast media

Method of collection of data:

The study was approved by the institutional review board. An informed consent was taken from all the patients for their willingness to participate in the study. Prior to entering the study individuals who were planned for CECT studies underwent renal function test (serum creatinine), which was considered as baseline recording. The various CECT studies performed were CECT abdomen, CECT thorax, CECT neck, CECT kidney ureter and bladder (KUB), CT pulmonary angiography, and CECT brain. Baseline demographic data was collected. History of CIN risk factors were also recorded, which included history of hypertension, renal insufficiency, age (age > 65 years was considered as high risk), chronic use of NSAIDs, and diabetes mellitus.

Assessment of CIN

Following the CECT study a repeat renal function test for serum creatinine was performed 48 to 72 hours after the CECT study. The patients in whom there was absolute (≥0.5 mg/dL) or relative (≥25%) rise in serum creatinine from baseline were considered as positive and these patients were followed up for a period of up to 11 days to assess short term outcome, which was return to baseline serum creatinine values (Figure 9). Individuals who were lost to follow-up were excluded in the final analysis.

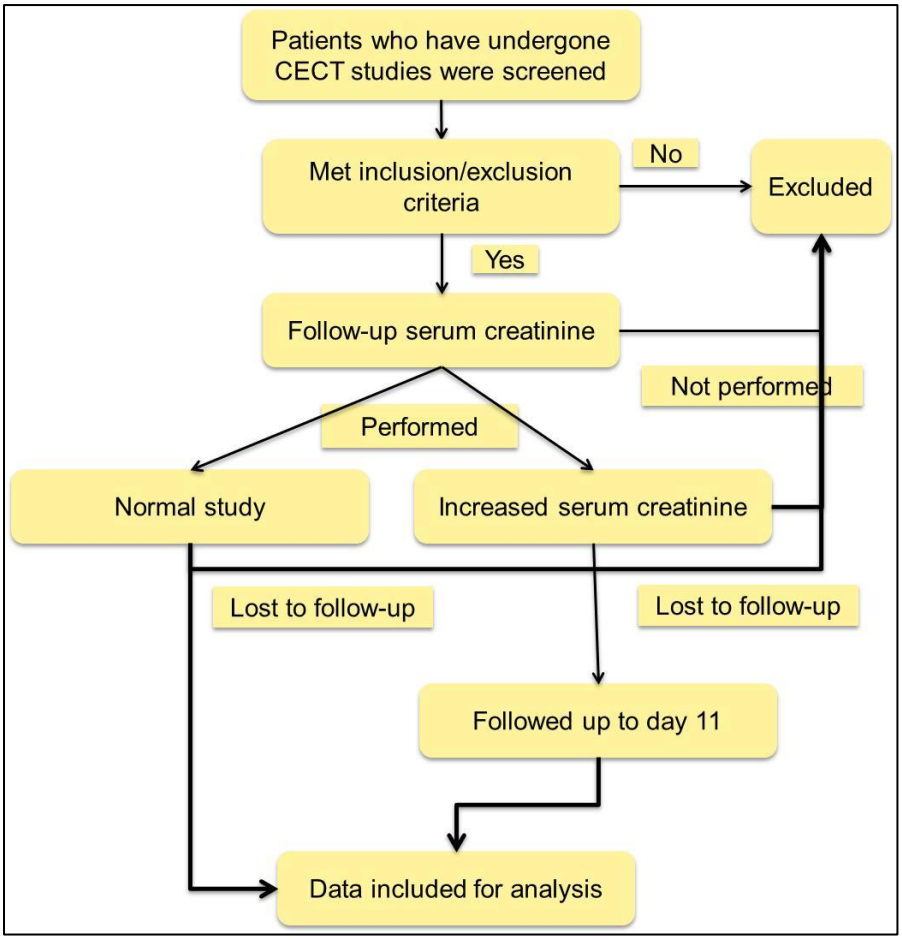

Figure 9. Study schematic

Statistical Analysis

Data was recorded into Microsoft® Excel® and was analyzed using OpenEpi® software. All the data were presented as mean ± SD. For radiation dose and mean mAs delivered, a paired t-test was performed to compare both the groups. Since each patient served as his/her own control, the results obtained in the standard-dose group was considered as standard and findings from low-dose group were compared with standard-dose group. Sensitivity and specificity for low-dose group was compared with results obtained from standard-dose group. A *P* value of <.05 was considered as statistically significant.

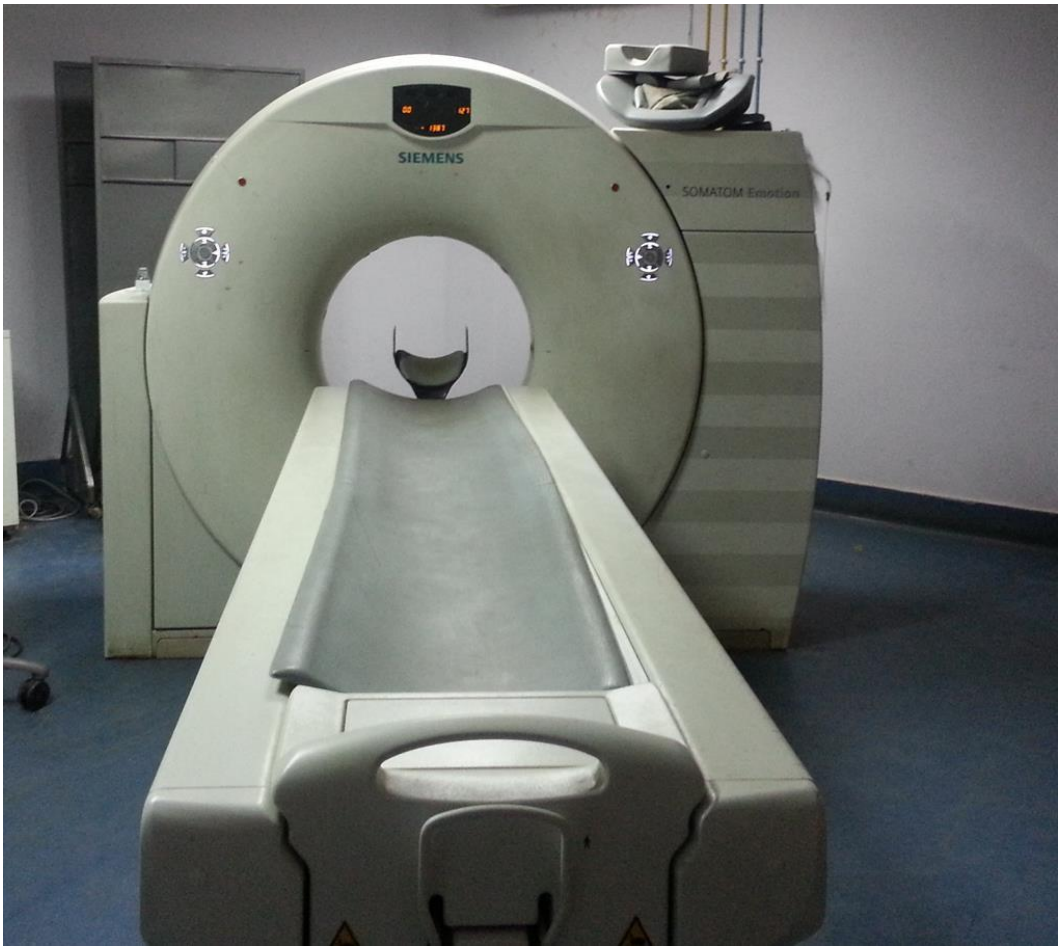

Figure 10. SIEMENS® SOMATOM EMOTION 16® CT scanner used in the study.

RESULTS

In our study we screened a total of 1028 patients who underwent CECT studies for various indications. Among them total of 734 patients met the inclusion and exclusion criteria and were short listed for the study. Among these patients 401 patients were outpatients who could not be followed up as they did not turn up for follow-up investigations. Of the remaining 333 patients, 23 patients refused to provide consent for participation in the study. There were 310 patients who were included in the final analysis (Figure 11).

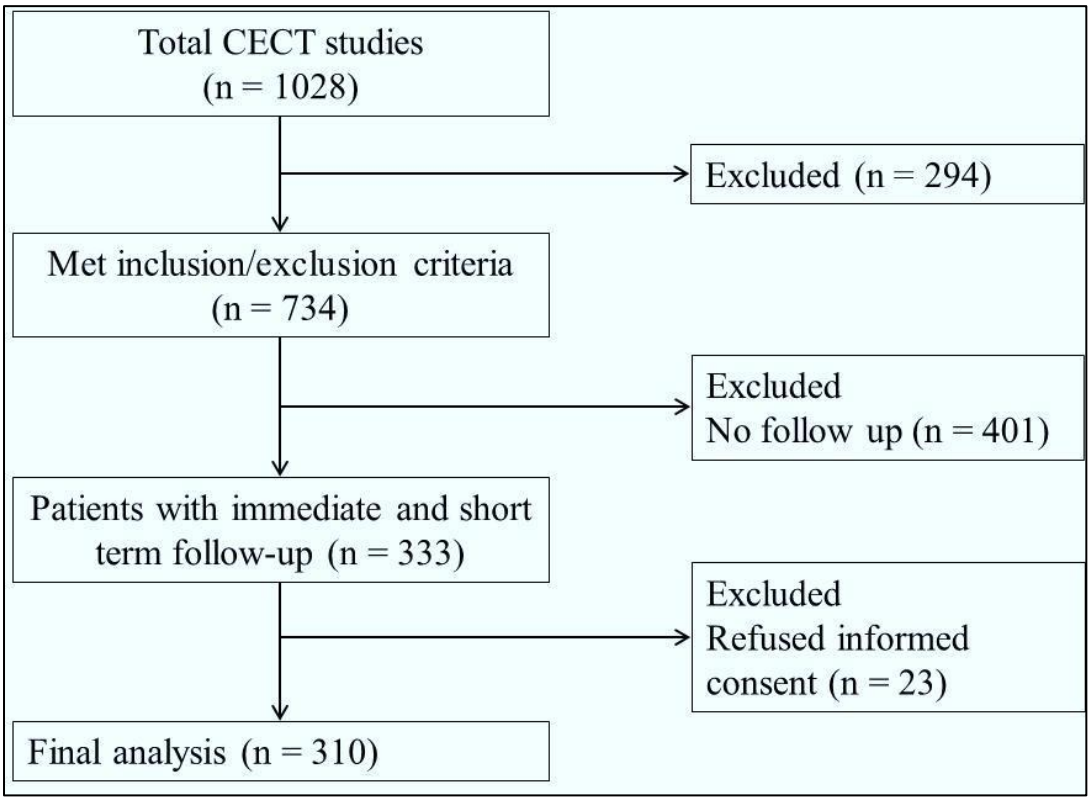

Figure 11. Flow chart showing screening of individuals for the study

Table 1. Gender-wise Distribution of Patients

Gender	Number of patients	%
Male	174	56.1
Female	136	43.9
Total	310	100

There were a total of 310 patients in our study. The mean age of patients in our study was 52.6 years ± 16.4 years (mean ± SD) (range 23 to 90 years). There was a slight male preponderance in our study (n = 174; 56.1%) (Table 1; Figure 12). The mean age of males was 51.09 ± 17.34 years (mean ± SD) and the mean age of females was 54.52 ± 14.9 years (mean ± SD), the difference of which was not statistically different (*P* = .06)

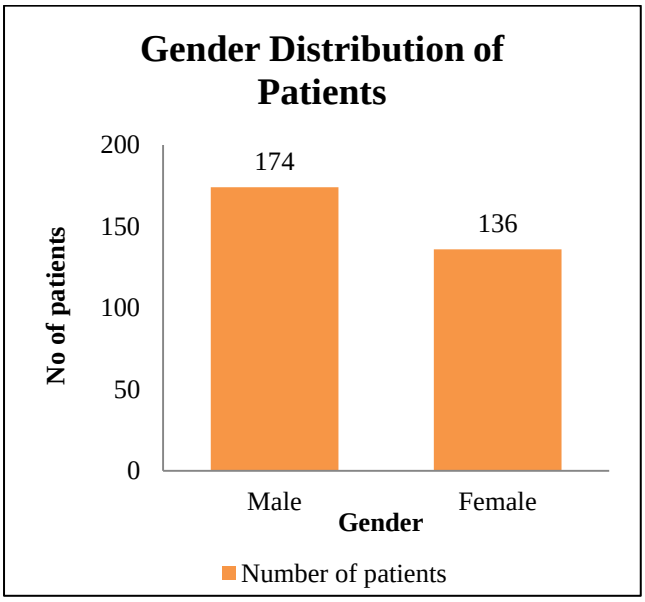

Figure 12. Gender-wise distribution of patients.

Table 2. Various CECT Examination Performed

Type of study	No of patients	%
CECT abdomen	111	35.81
CECT neck	80	25.81
CECT thorax	56	18.06
CECT KUB/ CT urography	31	10.00
CECT Brain	29	9.35
CE PA	3	0.97
Total	310	100

CECT = contrast enhanced computed tomography; KUB = kidney ureter bladder; PA = pulmonary angiography

The commonest contrast examination performed in our study was CECT abdomen in 111 patients (35.8%) followed by CECT neck (n = 80; 25.8%), CECT thorax (n = 56; 18.06%), CECT KUB/ CT urography (n = 31; 10%), CECT brain (n = 29; 9.35%) and lastly CE pulmonary angiogram (n = 3; 0.97%).

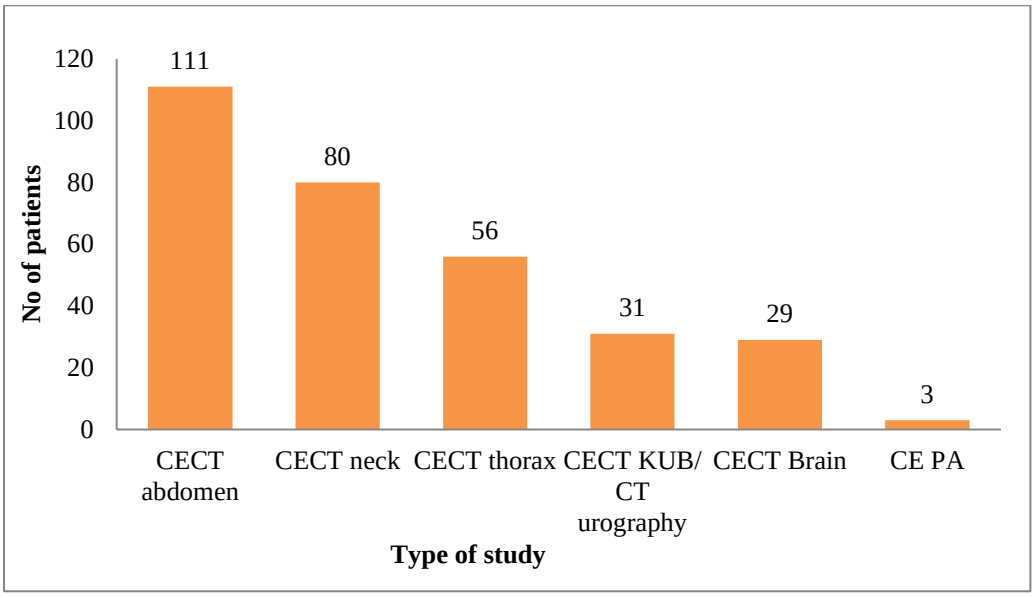

Figure 13. Various CECT examination performed (CECT contrast enhanced computed tomography; KUB = kidney ureter bladder; PA = pulmonary angiography).

Table 3. Risk Factors for CIN

Risk factor*	**No of patients**	**%**
Elderly†	67	21.6
Hypertension	30	9.7
Diabetes	26	8.4
NSAID use	10	3.2
Renal insufficiency	4	1.3
Total	137	44.19355

CIN = contrast induced nephropathy; NSAID = non-steroidal anti-inflammatory drug;

†elderly age was defined as age >65 years

*There were 72 patients with one risk factor, 25 patients with two risk factors and five patients with three risk factors

The mean serum initial serum creatinine level was 1.135 ± 0.163 mg/dL (mean ± SD) (range 0.8 to 1.5 mg/dL). The risk factors evaluated in our study were elderly (n = 67; 21.6%), hypertension (n = 30; 9.7%), diabetes mellitus (n = 26; 8.4%), NSAID use (n = 10; 3.2%) and renal insufficiency (n = 3; 1.3%). Risk factors were seen in total of 102 patients (32.9%). Among them, 72 patients (23.2%) had one risk factor followed by two risk factors in 25 patients (16.13%) and lastly five patients (4.84%) had three risk factors with total of 137 risk factors (Table 3; Figure 14).

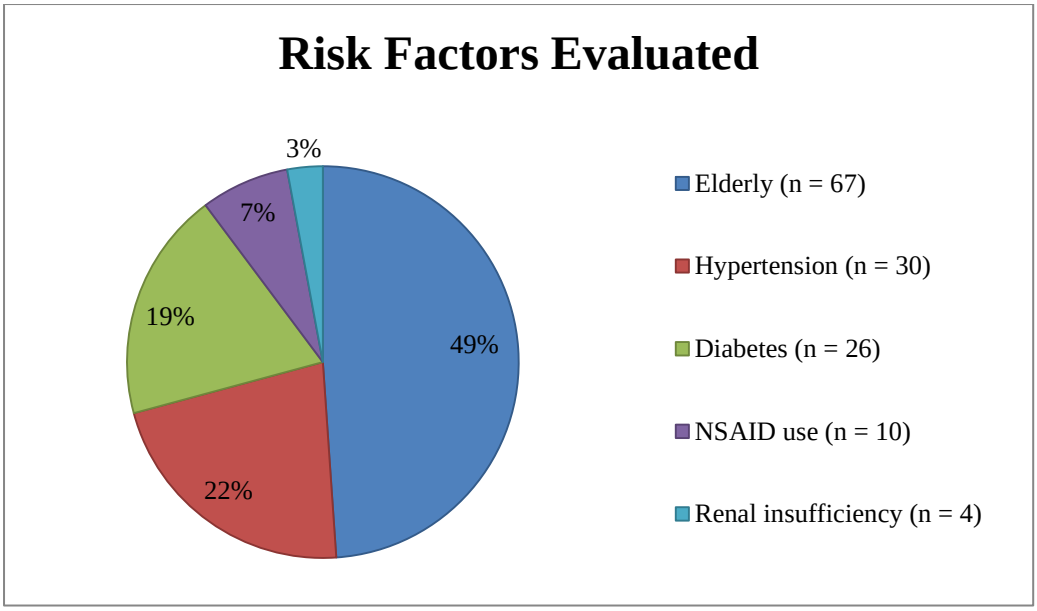

Figure 14. Risk factors for CIN evaluated in our study (elderly was defined as > 65 years; CIN = contrast induced nephropathy; NSAID = nonsteroidal anti-inflammatory drugs).

Table 4. Initial vs Post CECT Serum Creatinine Levels

	Serum creatinine level (mg/dL)				
	Initial		Post CECT		*P*
	Mean	SD	Mean	SD	
Elderly (n = 67)	1.149	0.479	1.267	0.526	*P* = .17
Hypertension (n = 30)	1.167	0.348	1.337	0.399	*P* = .08
Diabetes (n = 26)	1.135	0.318	1.306	0.365	*P* = .07
NSAID use (n = 10)	1.16	0.208	1.18	0.210	*P* = .8
Renal insufficiency (n = 4)	1.15	0.130	1.45	0.166	*P* = .026
Overall	1.13	0.163	1.25	0.170	

CECT = contrast enhanced computed tomography; NSAID = nonsteroidal anti-inflammatory drug; SD = standard deviation.

P<.05 considered significant

The mean initial serum creatinine levels were 1.13 ± 0.163 mg/dL (mean ± SD) and mean post CECT serum creatinine levels were 1.25 ± 0.17 mg/dL (mean ± SD). When patients with risk factors were considered, the mean initial serum creatinine levels were 1.149 ± 0.479 mg/dL (mean ± SD) in elderly individuals and mean post CECT serum creatinine levels were 1.267 ± 0.526 mg/dL (mean ± SD). The increase in serum creatinine level was not statistically significant (*P* = .17). Similarly the mean initial serum creatinine level in patients with hypertension was 1.167 ± 0.348 mg/dL (mean ± SD) and mean post CECT serum creatinine level was 1.337 ± 0.399 mg/dL (mean ± SD), which was not statistically significant (*P* = .08). The initial mean serum creatinine level in diabetics was 1.136 ± 0.318 mg/dL (mean ± SD)and post CECT serum creatinine level was 1.306 ± 0.365 mg/dL (mean ± SD), which was not statistically significant (*P* = .07) (Table 4). When patients with NSAID use were considered, the mean initial serum creatinine level was 1.16 ± 0.208 mg/dL (mean ± SD) and mean post CECT serum creatinine level was 1.18 ± 0.21 mg/dL

(mean ± SD) (*P* = .8). There was however, a statistically significant increase (*P* = .026) in the post CECT serum level in patients with renal insufficiency (initial mean serum creatinine level 1.15 ± 0.13 mg/dL (mean ± SD) and post CECT mean serum creatinine level 1.45 ± 0.166 mg/dL (mean ± SD) (Figure 15)). This difference could be attributed to the significant association in development of CIN in patients with renal insufficiency and that the sample size was limited, which could have biased our results.

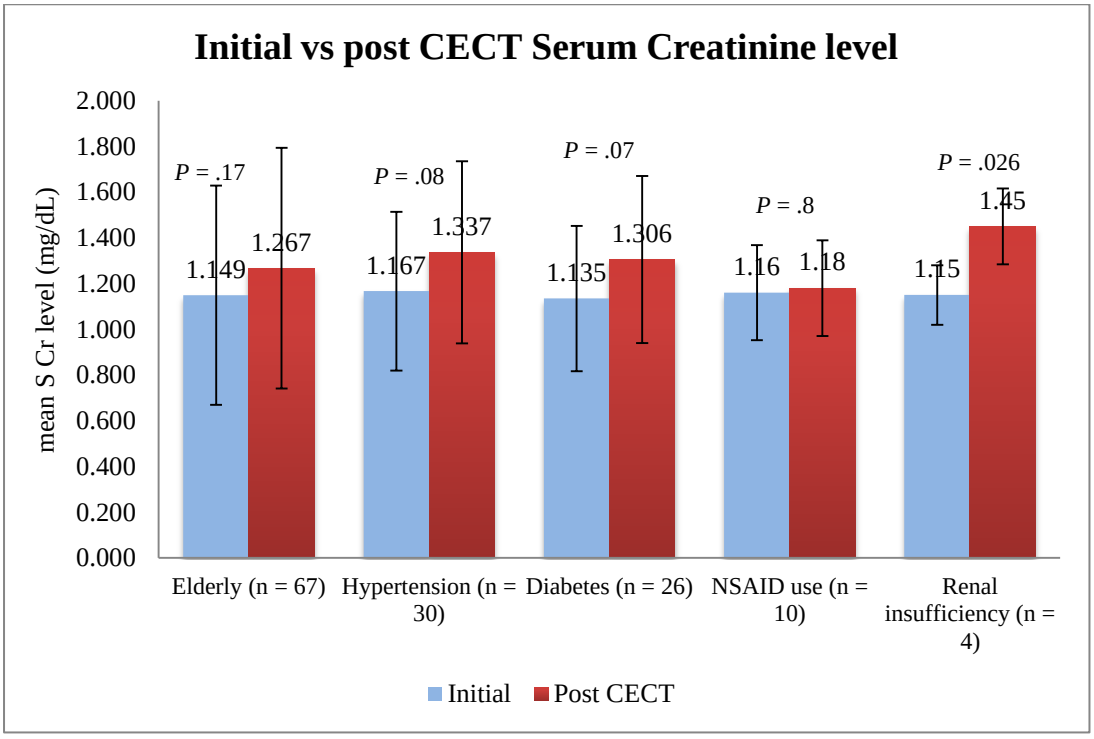

Figure 15. Initial vs post CECT mean serum creatinine levels

Table 5. Risk Factors in Patients with CIN

Risk Factors in CIN*	**No of patients**	**%**
Hypertension	5	1.61
Diabetes	4	1.29
Elderly†	4	1.29
Renal insufficiency	2	0.65
NSAID use	0	0.00
Total	15	4.84

CIN = contrast induced nephropathy; NSAID = non-steroidal anti-inflammatory drug;
†elderly age was defined as age >65 years
*10 patients had one risk factor and one patient each had two and three risk factors.

In our study CIN was observed in 12 patients (3.87%) all of whom had at least one risk factor. On follow up, CIN resolved in all patients by seven days without any complications. The risk factors were hypertension in five patients (1.61%), diabetes mellitus and elderly age group in four patients each (1.29%), renal insufficiency in two patients (0.65%). None of the patients with history of NSAID use developed CIN in our study. There were 10 patients with one risk factor (3.2%) and one patient had two risk factors (diabetes mellitus and hypertension) and one person had three factors (diabetes mellitus, elderly and hypertension) (0.3% each) (Table 5; Figure 16). Patients who developed CIN were treated with hydration and N-acetyl cysteine.

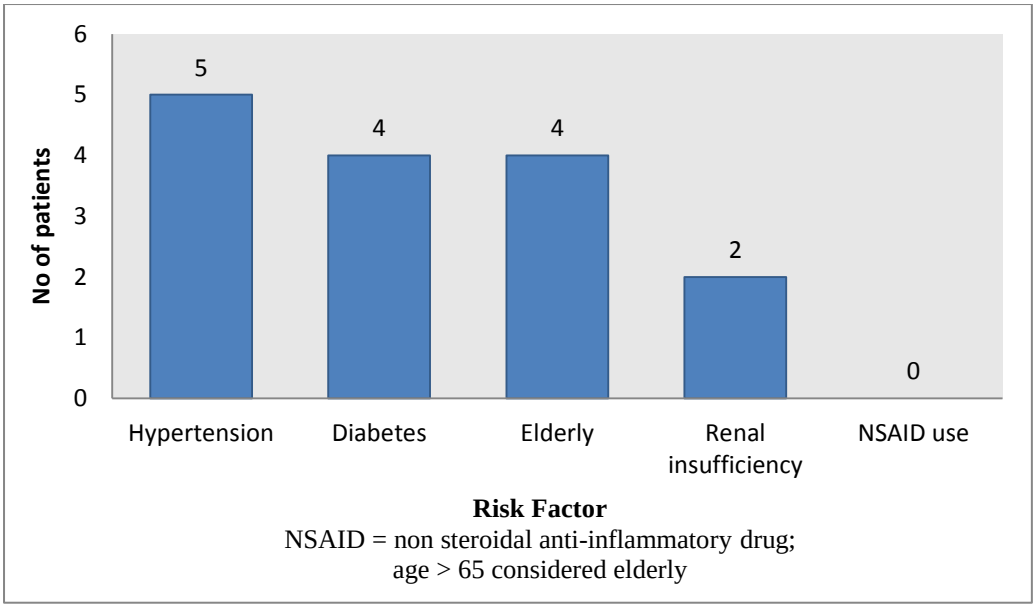

Figure 16. Risk factors in patients with CIN (Note: 10 patients had one risk factor; one patient each had two and three risk factors)

Table 6. Proportion of Patients with Risk Factors Developing CIN

Risk Factor	**CIN present**	**CIN absent**	**%**	**P**
Renal insufficiency	2	2	50	<0.001
Hypertension	5	25	16.67	<0.001
Diabetes	4	22	15.38	<0.001
Elderly*	4	63	5.97	0.001
NSAID use	0	10	0	NA

CIN = contrast induced nephropathy; NA = not applicable; NSAID = non-steroidal anti-inflammatory drug;
P = probability; Mid-P exact test
*Elderly age was defined as age >65 years

We further analyzed the proportion of patients with risk factors who developed CIN. We observed that patients with renal insufficiency had highest risk of developing CIN (50% risk; *P*<.001) followed by hypertension (five out of 30 patients; 16.67% risk; *P*<.001), diabetes mellitus (four out of 26 patients; 15.38%; *P*<.001) and lastly elderly age group (four out of 63 patients; 5.97%; *P* = .001). There were no patients with NSAID use who developed CIN. There was a significantly increased risk of developing CIN in patients with renal insufficiency, hypertension, diabetes mellitus and age >65 years. However, when compared with overall general population there was no statistically significant risk of developing CIN (Table 6, Figure 17).

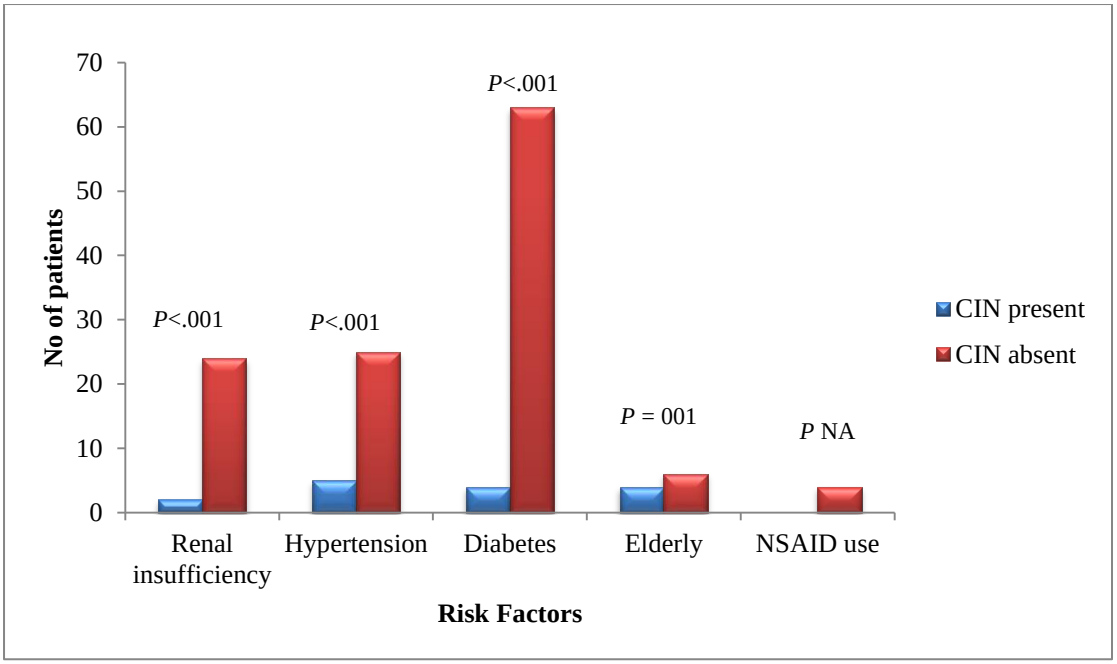

Figure 17. Proportion of Patients with Risk Factors developing CIN. CIN = contrast induced nephropathy; NSAID = non-steroidal anti-inflammatory drug, NA = not applicable. P compared with patients with no risk factors (Mid-P exact test).

DISCUSSION

Our study was designed for rural population who underwent CECT studies. There was a slight male preponderance in our study with males constituting 56.1%. The mean age of patients was 52.6 ± 16.4 years (mean ± SD) (range 23 to 90 years).

Our study population is similar to study by Bhatt et al. In their study in 250 patients, they found a male preponderance as compared with females (58.8% vs 41.2% respectively)[28]. Other studies have also shown a male preponderance[5] with very few studies showing a female predominance[34,35]. The studies which showed more female population in their baseline data had specific patient population such as patients with underlying carcinoma[34] or azotaemia[35].

Lee et al in their study of 140838 CT examinations also reported a similar age group as our study with the mean age being 57.9 ± 15.5 years[6]. However, Bhatt et al reported a lower age group of patients in their study with mean age of 41.41 ± 16.63 years (range 18 to 86 years)[28]. The difference in the mean age could perhaps be explained by the rural set up in our patients and urban set up in their study.

In our study the commonest contrast studies performed were CECT abdomen (35.81%) followed by CECT neck (25.81%) and CECT thorax (18.06%). The rest of studies combined constituted about 20% total studies performed (Table 2). This

pattern probably reflects the common indications seen in the rural set up. CECT abdomen is commonly performed for variety of indications, which include bowel obstruction, trauma, gastrointestinal (GI) and hepatobiliary (HPB) malignancies. CECT neck is commonly performed for head and neck cancers, which are very common in this region. Similarly, CECT thorax is commonly performed as lung infections and carcinoma lung. Recently CT urography is performed rather than intravenous urography and therefore it is seen at increasing frequency.

These findings are similar to findings reported by Baird et al, who reported CECT abdomen and pelvis and CECT chest in 35.5% of patient groups[32]. Similarly, Mitchell et al also reported a greater number of CECT abdomen and/or pelvis (54%) and CECT chest (27%) in their study[29]. These observations probably represent the cases seen in general practice.

We observed a low risk of CIN in our study (n = 12; 3.87%). All the patients with CIN had at least one risk factor. Data from various studies has showed varying incidence of CIN, based on the criteria used[1,5,6,18,20]. Our study was designed based on the widely used definition for CIN, which was defined as an absolute (≥ 0.5 mg/dL) or relative (≥ 25%) rise in serum creatinine from baseline at 48 to 72 hours[5,19,28]. We decided to use this criterion to define CIN as this was considered more specific, widely accepted by radiologists, easy to perform and calculate, and has less likelihood to yield false positive result and continues to remain as a commonly used definition and therefore can be easily reproducible[28,29,36,37,38].

There is a wide variability of incidence in literature ranging from 2.2% to >11%[4,5,6,33]. Lee et al reported 2.2% incidence of CIN in their large population based study in Korea[6]. Similarly, Moos et al in their large meta-analysis reported a variable incidence of CIN based on the criteria used. The authors reported that when criteria of relative increase in serum creative of ≥ 25% was used the incidence of CIN was 4.72%; when the criteria used was absolute increase of serum creatinine by ≥ 0.5 mg/dL, the incidence of CIN was 2.77%; when the criteria used was relative increase of serum creatinine by ≥ 25% or absolute increase of serum creatinine by ≥ 0.5 mg/dL the incidence of CIN was 4.96%[5]. A meta-analysis by Bhatt et al in tertiary hospital in North India, reported 10% risk of CIN in patients undergoing CECT studies. Furthermore, they also observed that risk of CIN was 10.7 in patients who received non-ionic contrast versus 7.9% in patients who received ionic contrast[28]. A higher risk of CIN was reported by Mitchell et al[29] and Rashid et al[33]. Our findings are similar to findings reported by Moos et al meta-analysis.

The risk factors evaluated in our study were elderly (n = 67; 21.6%), hypertension (n = 30; 9.7%), diabetes mellitus (n = 26; 8.4%), NSAID use (n = 10; 3.2%) and renal insufficiency (n = 3; 1.3%). Risk factors were seen in total of 102 patients (32.9%). Among them, 72 patients (23.2%) had one risk factor followed by two risk factors in 25 patients (16.13%) and lastly five patients (4.84%) had three risk factors with total of 137 risk factors.

Data from literature has shown a similar incidence of risk factors in patients undergoing CECT studying. Lee et al in their large population involving 140838 examinations in 101487 patients reported advanced age (>70 years) in 25.1% of cases, diabetes mellitus in 11.9% of patients, and hypertension in 13.7%. However, Lee et al reported a large number of users with NSAID usage (25.2%)[6], unlike our study, where it was only seen in 3.2% of patients. Some studies have reported a higher percentage of risk factors in patients undergoing CECT studies. A large meta-analysis by Moos et al reported diabetes in about 20.2% of the pooled data. Furthermore, they observed hypertension in 55.2% of the pooled data[5]. Similar observations were also made by Kooiman et al, who in their meta-analysis showed presence of diabetes in 28% of pooled data, hypertension in 19%, and chronic renal disease in 35%[27]. A similar incidence of risk factors was also reported by Kim et al, who in their study reported hypertension in >40% of patients and diabetes in >25% of patients[39]. The reason for wide variability of risk factors could be due to the characteristics in the native patient population and the type of studies going on. In our study, significant proportion of patients present with road traffic accidents or for evaluation of malignancy and it is possible that these patients may not have significant risk factors. It also probably the reason of high percentage of elderly in our population compared to other risk factors.

The mean initial serum creatinine levels were 1.13 ± 0.163 mg/dL (mean ± SD) and mean post CECT serum creatinine levels were 1.25 ± 0.17 mg/dL (mean ± SD). When patients with risk factors were considered, the mean initial serum creatinine levels were 1.149 ± 0.479 mg/dL (mean ± SD) in elderly individuals and mean post CECT serum creatinine levels were 1.267 ± 0.526 mg/dL (mean ± SD). The increase in serum creatinine level was not statistically significant (P = .17).

Similarly the mean initial serum creatinine level in patients with hypertension was 1.167 ± 0.348 mg/dL (mean ± SD) and mean post CECT serum creatinine level was 1.337 ± 0.399 mg/dL (mean ± SD), which was not statistically significant (P = .08). The initial mean serum creatinine level in diabetics was 1.136 ± 0.318 mg/dL (mean ± SD) and post CECT serum creatinine level was 1.306 ± 0.365 mg/dL (mean ± SD), which was not statistically significant (P = .07) (Table 4). When patients with NSAID use were considered, the mean initial serum creatinine level was 1.16 ± 0.208 mg/dL (mean ± SD) and mean post CECT serum creatinine level was 1.18 ± 0.21 mg/dL (mean ± SD) (P = .8). There was however, a statistically significant increase (P = .026) in the post CECT serum level in patients with renal insufficiency (initial mean serum creatinine level 1.15 ± 0.13 mg/dL (mean ± SD) and post CECT mean serum creatinine level 1.45 ± 0.166 mg/dL (mean ± SD)). This difference could be attributed to the significant association in development of CIN in patients with renal insufficiency and the limited sample size, which could have biased our results. We further analyzed the proportion of patients with risk factors who developed CIN. We observed that patients with renal insufficiency had highest risk of developing CIN (50% risk; P<.001) followed by hypertension (five out of 30 patients; 16.67% risk; P<.001), diabetes mellitus (four out of 26 patients; 15.38%; P<.001) and lastly elderly age group (four out of 63 patients; 5.97%; P = .001). There were no patients with NSAID use who developed CIN. There was a significantly increased risk of developing CIN in patients with renal insufficiency, hypertension, diabetes mellitus and age >65 years. However, when compared with overall general population there was no statistically significant risk of developing CIN.

Our findings are in agreement with data reported in literature. Moos et al have shown that diabetes significantly increases the risk for developing CIN with an odds ratio (OR) of 1.87 (95% CI: 1.55 to 2.26) (P<.001). They also observed that elderly individuals (age > 65 years) have a significantly higher risk of developing CIN with an OR of 1.95 (95% CI: 1.02 to 3.70) (P = .04). Renal insufficiency was also associated with significantly increased risk of CIN with highest OR of 4.1 (95%: 2.26 to 7.42) (P<.05). A significantly increased risk of CIN was also observed with chronic NSAID use (P = .04). The authors however did not find a significantly increased risk of CIN in patients with hypertension OR 1.33 (95% CI: 0.91 to 1.95; P = .13)[5]. Kooiman et al also reported an increased risk of CIN in patients with diabetes mellitus (9.3% vs 3.7% in patients with and without diabetes respectively; P<.001), chronic kidney disease (8.8% vs 5.2 in patients with and without chronic kidney disease respectively; P<.001)[27]. Lee et al also observed a increased risk of developing CIN in patients with history of diabetes mellitus, hypertension, advanced age (≥ 70 years), used of NSAIDS and in patients with reduced renal function (renal insufficiency) with RR of 1.5 (95% CI: 1.35 to 1.66), 1.37 (95% CI: 1.24 to 1.51), 1.36 (95% CI:1.25 to 1.47), 1.07 (95% CI: 0.98 to 1.16) and 12.99 (95% CI: 11.92 to 14.17) respectively. They did not find significantly increased with NSAID use on multivariate analysis[6], which is consistent with our finding. In our study, hypertension was associated with increased risk of CIN, which was not observed in some studies. The reason for variability of risk factors is not entirely understood. Although we observed hypertension as risk factor for CIN, it was not reported by Moos et al[5]. Similarly, Moos et al reported risk of CIN with use of NSAIDs, which was not observed in our study or in meta-analysis by Moos et al[5,27]. The most consistent risk factors include diabetes mellitus, hypertension and advanced age in most of studies[5,6,27].

The exact mechanism for CIN is not completely understood and it is believed to be caused due to myriad factors that ultimately play a role in deterioration of renal function. CIN is believed to result from direct damage to renal tubules and hypoxia induced damage to medullary portion of kidney[21-23,27]. There are four primary mechanisms, which are considered to contribute to development of CIN. Initially, there is endothelium-independent transient vasodilation following contrast injection, which results in release of endothelin, adenosine and various other renal vasoconstrictors. This results in renal vasoconstriction reducing renal blood supply. It is believed that contrast medium induced vasoconstriction results in renal hypoxia (reduced blood flow). This further results in spiraling reaction causing further loss of renal autoregulation, which in turn leads to reduced blood flow to outer renal medulla. This in turn results in generation of reactive oxygen species due to reduced renal blood flow and contrast media toxicity, which exceeds the normal anti-oxidant reserve of kidneys causing further renal hypoxia. It is also believed that contrast media in itself can cause direct cytotoxic effect on renal tubules resulting in renal hypoxia[22-27]. It is for this reason that there is an increased risk of CIN in patients with renal insufficiency. It is also believed that diabetes mellitus results in disturbed renal autoregulation, predisposing diabetics for risk of developing CIN[27]. Diabetics are hypothesized to have wide variations in serum creatinine levels following contrast administration and this might be the result of higher incidence of CIN. It is possible the findings may reflect this variation in serum creatinine rather than CIN or renal damage. There is also an argument that the increased risk of CIN could possibly due to use of high osmolar contrast agents, primarily used in cardiac catheterizations and may not be true with the currently used low- or iso-osmolar contrast media, used for

CECT studies[40]. Some authors have argued that the current observational and retrospective studies evaluating risk of CIN and renal injury may not be sufficient understand the true risk posed by CIN on mortality and morbidity. Most of the studies in the literature don't have a control group and therefore, data from comparative studies using a control group may be needed. One can also argue that in general practice patients are generally followed up after CECT and this may affect the true incidence of CIN. Furthermore, patients who are hospitalized usually have one or more risk factors for CIN and this may result in skewed data on risk of CIN. These patients are also at increased risk of mortality and morbidity due to underlying disease conditions and makes causality of CIN difficult if not impossible. Further data is needed to evaluate the true risk of CIN with iodinated contrast media[40,41]. Until we determine the exact relation between use of contrast media and development of CIN, the current data strongly supports the observation that iodinated contrast media increases the risk of CIN and that the risk factors for CIN are diabetes mellitus, hypertension, advancing age (>65 years), and renal insufficiency[27,41].

Our study has certain limitations. We did not a control group in our study and our study was observational in nature. Secondly our sample was relatively smaller considering some of the large databases reported in literature. We also had fewer patients with renal insufficiency who underwent CECT study as these patients are usually not taken up for contrast studies. A greater number of patients with renal insufficiency would have been ideal. Also history of NSAID use in our population tends to be inaccurate as patients prescribed long-tern NSAIDs seldom take them. We did not evaluate the long-term impact of CECT study. Also many patients who

undergo CECT studies come on OPD basis and follow-up may not be possible in those patients, thus skewing our data towards inpatients.

CONCLUSION

We observed a modest risk of CIN following CECT studies. The risk factors for developing CIN were diabetes mellitus, elderly age (>65 years), hypertension and renal insufficiency. Serum creatinine levels reached baseline in all the patients who developed CIN within a week. We concluded that use of non-ionized iodinated contrast media is associated with low risk of CIN and that CECT studies do not cause significant increase in CIN. Further studies with control group may be needed to quantify exact risk of iodinated contrast media for developing CIN.

SUMMARY

Contrast media have increasingly been employed in most of the computed tomographic (CT) studies. Contrast induced nephropathy (CIN) is considered as a major adverse event following intravenous iodinated contrast use. The most commonly used definition of CIN is an absolute (≥ 0.5 mg/dL) or relative (≥25%) rise in serum creatinine from baseline within 48 to 72 hours.

The aims of the study were to determine the incidence of contrast induced nephropathy following use of non-ionic contrast used in contrast enhanced computed tomographic studies and to identify the risk factors that can predispose development of contrast induced nephropathy

This descriptive observational study was carried out over a period of 18 months from January 2017 to June 2018 in 310 patients who underwent CECT. Renal function analysis was done based on serum creatinine which were performed prior to CECT and between 24- 48 hours after CECT of Radio-Diagnosis, R. L. Jalappa Hospital & Research Centre.

In our study we screened a total of 1028 patients who underwent CECT studies for various indications. Among them total of 734 patients met the inclusion and exclusion criteria and were short listed for the study. Among these patients 401 patients were outpatients who could not be followed up as they did not turn up for follow-up investigations. Of the remaining 333 patients, 23 patients refused to provide

consent for participation in the study. There were 310 patients who were included in the final analysis.

There were a total of 310 patients in our study. The mean age of patients in our study was 52.6 years ± 16.4 years (mean ± SD) (range 23 to 90 years). There was a slight male preponderance in our study (n = 174; 56.1%). The mean age of males was 51.09 ± 17.34 years (mean ± SD) and the mean age of females was 54.52 ± 14.9 years (mean ± SD), the difference of which was not statistically different (*P* = .06).

The commonest contrast examination performed in our study was CECT abdomen in 111 patients (35.8%) followed by CECT neck (n = 80; 25.8%), CECT thorax (n = 56; 18.06%), CECT KUB/ CT urography (n = 31; 10%), CECT brain (n = 29; 9.35%) and lastly CE pulmonary angiogram (n = 3; 0.97%).

The risk factors evaluated in our study were elderly (n = 67; 21.6%), hypertension (n = 30; 9.7%), diabetes mellitus (n = 26; 8.4%), NSAID use (n = 10; 3.2%) and renal insufficiency (n = 3; 1.3%). Risk factors were seen in total of 102 patients (32.9%). Among them, 72 patients (23.2%) had one risk factor followed by two risk factors in 25 patients (16.13%) and lastly five patients (4.84%) had three risk factors with total of 137 risk factors.

The mean initial serum creatinine levels were 1.13 ± 0.163 mg/dL (mean ± SD) and mean post CECT serum creatinine levels were 1.25 ± 0.17 mg/dL (mean ± SD). When patients with risk factors were considered, the mean initial serum creatinine levels were 1.149 ± 0.479 mg/dL (mean ± SD) in elderly individuals and

mean post CECT serum creatinine levels were 1.267 ± 0.526 mg/dL (mean ± SD). The increase in serum creatinine level was not statistically significant (P = .17). Similarly the mean initial serum creatinine level in patients with hypertension was 1.167 ± 0.348 mg/dL (mean ± SD) and mean post CECT serum creatinine level was 1.337 ± 0.399 mg/dL (mean ± SD), which was not statistically significant (P = .08). The initial mean serum creatinine level in diabetics was 1.136 ± 0.318 mg/dL (mean ± SD) and post CECT serum creatinine level was 1.306 ± 0.365 mg/dL (mean ± SD), which was not statistically significant (P = .07) (Table 4). When patients with NSAID use were considered, the mean initial serum creatinine level was 1.16 ± 0.208 mg/dL (mean ± SD) and mean post CECT serum creatinine level was 1.18 ± 0.21 mg/dL (mean ± SD) (P = .8). There was however, a statistically significant increase (P = .026) in the post CECT serum level in patients with renal insufficiency (initial mean serum creatinine level 1.15 ± 0.13 mg/dL (mean ± SD) and post CECT mean serum creatinine level 1.45 ± 0.166 mg/dL (mean ± SD)). This difference could be attributed to the significant association in development of CIN in patients with renal insufficiency and that the sample size was limited, which could have biased our results.

In our study CIN was observed in 12 patients (3.87%) all of whom had at least one risk factor. On follow up, CIN resolved in all patients by seven days without any complications. The risk factors were hypertension in five patients (1.61%), diabetes mellitus and elderly age group in four patients each (1.29%), renal insufficiency in two patients (0.65%). None of the patients with history of NSAID use developed CIN in our study. There were 10 patients with one risk factor (3.2%) and one patient had two risk factors (diabetes mellitus and hypertension) and one person had three factors

(diabetes mellitus, elderly and hypertension) (0.3% each). Patients who developed CIN were treated with hydration and N-acetyl cysteine.

We further analyzed the proportion of patients with risk factors who developed CIN. We observed that patients with renal insufficiency had highest risk of developing CIN (50% risk; $P<.001$) followed by hypertension (five out of 30 patients; 16.67% risk; $P<.001$), diabetes mellitus (four out of 26 patients; 15.38%; $P<.001$) and lastly elderly age group (four out of 63 patients; 5.97%; $P = .001$). There were no patients with NSAID use who developed CIN. There was a significantly increased risk of developing CIN in patients with renal insufficiency, hypertension, diabetes mellitus and age >65 years. However, when compared with overall general population there was no statistically significant risk of developing CIN

We observed a modest risk of CIN following CECT studies. The risk factors for developing CIN were diabetes mellitus, elderly age (>65 years), hypertension and renal insufficiency. Serum creatinine levels reached baseline in all the patients who developed CIN within a week. We concluded that use of non-ionized iodinated contrast media is associated with low risk of CIN and that CECT studies do not cause significant increase in CIN.

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ANNEXURE -I

PROFORMA

INCIDENCE OF CONTRAST INDUCED NEPHRO PATHY FOLLOWING INTRAVENOUS CONTRAST ENHANCED COMPUTED TOMOGRAPHY

PROFORMA

Demographic details:

Name:

Age:

Clinical History:

Initial serum creatinine value:

Post CECT serum creatinine value:

Significant change in serum creatinine (Y/N)

Treatment administered (if any):

Final outcome:

ANNEXURE-II

INFORMED CONSENT FORM

Study title: **INCIDENCE OF CONTRAST INDUCED NEPHROPATHY FOLLOWING INTRAVENOUS CONTRAST ENHANCED COMPUTED TOMOGRAPHY**

Chief researcher/ PG guide's name: Dr. N. RACHEGOWDA

Principal investigator: Dr. NISHI KANT

Name of the subject:

Age :

Gender :

1. I have been informed in my own language that this study involves CT and use of contrast material as part of procedure. I have been explained thoroughly and understand its complication and possible side effects.
2. I understand that the medical information produced by this study will become part of institutional record and will be kept confidential by the said institute.
3. I understand that my participation is voluntary and may refuse to participate or may withdraw my consent and discontinue participation at any time without prejudice to my present or future care at this institution.
4. I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s).
5. I confirm that _____ (chief researcher/ name of PG guide) has explained to me the purpose of research and the study procedure that I will undergo and the possible risks and discomforts that i may experience, in my own language. I hereby agree to give valid consent to participate as a subject in this research project.

Participant’s signature/thumb impression

Signature of the witness: Date:

1)

2)

I have explained to _____ (subject) the purpose of the research, the possible risk and benefits to the best of my ability.

Chief Researcher/ Guide signature Date:

INCIDENCE OF CONTRAST INDUCED NEPHROPATHY FOLLOWING INTRAVENOUS CONTRAST ENHANCED COMPUTED TOMOGRAPHY

Patient Information Sheet

Principal Investigator: Dr. NISHI KANT/ Dr. N. RACHEGOWDA

I, Dr. Nishi Kant, post-graduate student in Department of Radio-Diagnosis at Sri Devaraj Urs Medical College. I will be conducting a study titled "INCIDENCE OF CONTRAST INDUCED NEPHROPATHY FOLLOWING INTRAVENOUS CONTRAST ENHANCED COMPUTED TOMOGRAPHY" for my dissertation under the guidance of Dr. N. Rachegowda, Professor, Department of Radio-Diagnosis. In this study, we will assess the change in blood serum creatinine levels after get contrast enhanced CT study done. There will be no additional expenses incurred by you for this test as it performed free of cost for you. You will not be paid any financial compensation for participating in this research project.

All of your personal data will be kept confidential and will be used only for research purpose by this institution. You are free to participate in the study. You can also withdraw from the study at any point of time without giving any reasons whatsoever. Your refusal to participate will not prejudice you to any present or future care at this institution

Name and Signature of the Principal Investigator

Date

ANNEXURE III

KEY TO MASTER CHART

CE PA = contrast enhanced

CT pulmonary angiogram

CECT = contrast enhanced computed tomography

dL = deciliter

DM = diabetes mellitus

F = female

HTN = hypertension

kg = kilogram

KUB = kidney, ureter and bladder

M = male

mg = milligram

NAC = N acetyl cysteine

NS = not significant

NSAID = non-steroidal anti-inflammatory drugs

R = recovered

RI = renal insufficiency

S = significant

Masterchart

Sl. No	Trial ID	Age	Sex		Risk factor					Type of study	Serum creatinine (mg/dL)			Follow-up	Treatment	Outcome
				Body weight (in kg)	DM	HTN	Elderly	NSAID use	RI		Initial	At 48-72 hours	Change (S/NS)			
1	467511	46	M	60	N	N	N	Y	N	CECT neck	1.3	1.3	NS			
2	73889	65	F	65	N	N	N	Y	N	CECT neck	1.2	1.3	NS			
3	628156	70	F	75	N	N	Y	N	Y	CECT neck	1.3	1.4	NS			
4	260275	28	M	61	N	N	N	N	N	CECT neck	1.2	1.1	NS			
5	322107	50	F	57	N	N	N	N	N	CECT neck	1.2	1.3	NS			
6	717486	27	M	64	N	N	N	Y	N	CECT neck	1.1	1.3	NS			
7	129504	49	M	61	N	N	N	N	N	CECT neck	1.2	1.3	NS			
8	641028	61	M	70	N	N	N	Y	Y	CECT neck	0.9	1.1	NS			
9	844472	46	F	52	N	N	N	N	N	CECT abdomen	1.1	1.3	NS			
10	746514	60	M	78	Y	Y	N	N	Y	CECT abdomen	1.2	1.3	NS			
11	9835	50	F	61	N	N	N	N	N	CECT abdomen	1.4	1.3	NS			
12	520713	50	F	55	N	N	N	N	N	CECT abdomen	0.8	0.9	NS			
13	740158	65	M	65	N	N	N	N	N	CECT abdomen	1.4	1.45	NS			
14	963307	90	M	58	N	Y	Y	N	N	CECT abdomen	1.2	1.32	NS			
15	176114	75	M	60	N	N	Y	N	N	CECT abdomen	1	1.1	NS			
16	312121	75	F	59	N	N	Y	N	N	CECT abdomen	1.2	1.4	NS			
17	270307	66	M	65	N	N	Y	N	N	CECT abdomen	1.1	1	NS			
18	343911	54	F	59	N	N	N	N	N	CECT abdomen	1.4	1.3	NS			
19	387725	56	M	65	N	N	N	N	N	CECT KUB	1.4	1.45	NS			
20	735904	47	M	67	N	Y	N	N	Y	CECT KUB	1.1	1.3	NS			
21	914558	65	M	79	N	N	N	N	Y	CECT KUB	1.3	1.1	NS			
22	74653	63	M	72	N	N	N	N	Y	CECT KUB	1.2	1.2	NS			
23	37224	23	M	74	N	N	N	N	Y	CECT KUB	1.1	1.3	NS			
24	203878	67	F	65	N	N	Y	N	N	CECT KUB	1.3	1.4	NS			
25	157688	47	M	77	N	N	N	N	Y	CECT KUB	1.2	1.3	NS			
26	519520	63	M	59	N	N	N	N	N	CECT KUB	0.9	1.1	NS			
27	47170	28	M	65	N	N	N	N	N	CECT KUB	0.8	0.95	NS			
28	13190	39	M	57	N	N	N	N	N	CECT KUB	1.2	1.3	NS			
29	47414	45	M	65	Y	Y	N	N	N	CECT thorax	1	1.1	NS			
30	157206	55	M	68	N	N	N	N	Y	CECT thorax	0.98	1.2	NS			
31	596848	76	F	59	N	N	Y	N	N	CECT thorax	0.8	1.2	S	45	Hydration	R
32	811485	50	F	62	N	Y	N	N	N	CECT thorax	1.2	1.3	NS			
33	490536	65	M	69	N	N	N	N	Y	CECT thorax	1.1	1.2	NS			
34	998854	75	F	59	Y	N	Y	N	N	CECT thorax	1.2	1.25	NS			
35	708485	48	M	68	N	N	N	N	Y	CECT thorax	1.1	1.2	NS			
36	659460	50	M	71	N	N	N	N	Y	CECT thorax	0.95	1.1	NS			
37	509758	78	M	68	N	N	Y	N	Y	CECT thorax	1.2	1.3	NS			

CE PA = contrast enhanced CT pulmonary angiogram, CECT = contrast enhanced computed tomography ,dL = deciliter, DM = diabetes mellitus, F = female, HTN = hypertension, kg = kilogram, KUB = kidney, ureter and bladder, M = male, mg = milligram, NAC = N acetyl cysteine, NS = not significant, NSAID = non-steroidal anti-inflammatory drugs, R = recovered, RI = renal insufficiency, S = significant

Sl. No	Trial ID	Age	Sex		Risk factor					Type of study	Serum creatinine (mg/dL)			Follow-up	Treatment	Outcome
				Body weight (in kg)	DM	HTN	Elderly	NSAID use	RI		Initial	At 48-72 hours	Change (S/NS)			
38	184502	79	F	61	Y	N	Y	N	N	CECT thorax	0.8	0.9	NS			
39	823331	24	M	65	N	N	N	N	N	CECT abdomen	1.1	1.3	NS			
40	282823	85	F	55	Y	N	Y	N	N	CECT abdomen	0.9	1.2	S	45	Hydration	R
41	954351	29	F	75	N	N	N	N	Y	CECT abdomen	1.1	1.2	NS			
42	500793	65	F	70	N	N	N	Y	Y	CECT abdomen	0.8	0.9	NS			
43	495557	62	F	68	N	Y	N	N	Y	CECT abdomen	1.2	1.3	NS			
44	91721	52	M	61	N	N	N	N	N	CECT abdomen	1.2	1.1	NS			
45	735308	67	F	70	N	Y	Y	N	Y	CECT abdomen	1.3	1.4	NS			
46	672495	40	F	80	N	N	N	N	Y	CECT abdomen	0.95	1.1	NS			
47	333635	48	F	75	N	N	N	N	Y	CECT abdomen	1.3	1.4	NS			
48	710631	55	F	82	N	N	N	N	Y	CECT abdomen	1.1	1.2	NS			
49	96665	28	M	79	N	N	N	N	Y	CECT neck	1.4	1.3	NS			
50	991518	30	M	69	N	N	N	N	Y	CECT neck	1.1	1.1	NS			
51	20604	46	M	68	N	Y	N	N	Y	CECT neck	0.9	1	NS			
52	571359	60	M	63	N	N	N	N	N	CECT neck	0.9	1	NS			
53	890331	45	F	72	N	N	N	N	Y	CECT neck	1.3	1.2	NS			
54	36398	58	F	67	N	N	N	N	Y	CECT neck	1.3	1.4	NS			
55	200790	41	M	76	N	N	N	N	Y	CECT neck	1	1.2	NS			
56	42518	71	M	65	N	N	Y	N	N	CECT neck	1.2	1.3	NS			
57	108442	45	M	78	N	N	N	N	Y	CECT neck	0.8	0.9	NS			
58	259387	64	M	60	N	N	N	N	N	CECT neck	1	1.1	NS			
59	930514	60	F	61	N	N	N	N	N	CECT neck	0.9	1	NS			
60	801520	55	M	74	N	N	N	N	Y	CECT neck	1.1	1	NS			
61	761315	57	M	82	N	N	N	N	Y	CECT neck	1.2	1.2	NS			
62	103572	75	F	65	N	N	Y	N	N	CECT neck	1.1	1.2	NS			
63	633873	20	M	64	N	N	N	N	N	CECT neck	1.2	1.2	NS			
64	363275	20	M	63	N	N	N	N	N	CECT neck	0.9	1.1	NS			
65	547422	46	F	74	N	N	N	N	Y	CECT neck	1.1	1.2	NS			
66	371725	62	M	61	N	N	N	N	N	CECT neck	0.85	0.9	NS			
67	787394	65	M	71	N	N	N	N	Y	CECT abdomen	0.9	1	NS			
68	81602	30	M	75	N	N	N	N	Y	CECT abdomen	1	1.2	NS			
69	27231	52	M	74	N	N	N	N	Y	CECT abdomen	1.2	1.3	NS			
70	429498	47	M	69	N	N	N	N	Y	CECT abdomen	0.9	1.1	NS			
71	14448	75	M	74	N	Y	Y	N	Y	CECT abdomen	1.3	1.2	NS			
72	286915	65	F	68	N	N	N	N	Y	CECT abdomen	1.2	1.25	NS			
73	401403	38	M	83	N	N	N	N	Y	CECT abdomen	0.9	1.1	NS			
74	251806	65	M	74	N	N	N	N	Y	CECT abdomen	0.9	1.1	NS			
75	856923	70	M	68	Y	N	Y	N	Y	CECT abdomen	1.3	1.2	NS			
76	514097	69	M	84	N	N	Y	N	Y	CECT abdomen	1.4	1.45	NS			

CE PA = contrast enhanced CT pulmonary angiogram, CECT = contrast enhanced computed tomography ,dL = deciliter, DM = diabetes mellitus, F = female, HTN = hypertension, kg = kilogram, KUB = kidney, ureter and bladder, M = male, mg = milligram, NAC = N acetyl cysteine, NS = not significant, NSAID = non-steroidal anti-inflammatory drugs, R = recovered, RI = renal insufficiency, S = significant

Sl. No	Trial ID	Age	Sex		Risk factor					Type of study	Serum creatinine (mg/dL)			Follow-up	Treatment	Outcome
				Body weight (in kg)	DM	HTN	Elderly	NSAID use	RI		Initial	At 48-72 hours	Change (S/NS)			
77	679897	70	M	78	N	N	Y	N	Y	CECT abdomen	0.8	0.9	NS			
78	427966	60	F	71	N	N	N	N	Y	CECT abdomen	0.9	1.1	NS			
79	893655	52	F	68	N	N	N	N	Y	CECT abdomen	1.3	1.4	NS			
80	421055	63	M	73	N	N	N	N	Y	CECT abdomen	1.4	1.45	NS			
81	751520	38	F	75	N	N	N	N	Y	CECT abdomen	1.3	1.2	NS			
82	513606	40	F	65	N	N	N	N	N	CECT abdomen	1.4	1.5	NS			
83	952885	21	F	64	N	N	N	N	N	CECT abdomen	1.4	1.3	NS			
84	395797	40	M	61	N	Y	N	N	N	CECT Brain	1.2	1.28	NS			
85	713663	55	M	78	N	N	N	N	Y	CECT Brain	1.2	1.3	NS			
86	191908	59	M	80	Y	Y	N	N	Y	CECT Brain	1.4	1.4	NS			
87	652889	28	M	82	N	N	N	Y	Y	CECT Brain	1.3	1.2	NS			
88	514841	22	M	79	N	N	N	N	Y	CECT Brain	1.1	1.2	NS			
89	875863	44	F	77	N	Y	N	N	Y	CECT Brain	1.2	1.4	NS			
90	668464	26	F	59	N	N	N	N	N	CECT Brain	1	1.1	NS			
91	900341	70	M	68	N	N	Y	N	Y	CECT abdomen	1.2	1.1	NS			
92	336356	70	M	65	N	N	Y	N	N	CECT abdomen	1.3	1.3	NS			
93	421532	67	F	60	N	N	Y	Y	N	CECT abdomen	1.4	1.3	NS			
94	875375	55	F	61	N	N	N	N	N	CECT abdomen	1.4	1.4	NS			
95	788709	45	M	69	N	N	N	N	Y	CECT abdomen	1.3	1.4	NS			
96	811062	21	M	59	N	N	N	N	N	CECT abdomen	1.2	1.4	NS			
97	778432	26	M	58	N	N	N	N	N	CECT abdomen	1.4	1.4	NS			
98	635786	62	F	62	N	N	N	Y	N	CECT abdomen	1.4	1.2	NS			
99	775553	45	F	59	N	N	N	N	N	CECT abdomen	1.2	1.3	NS			
100	553380	29	M	68	N	N	N	N	Y	CECT abdomen	1.3	1.2	NS			
101	986995	48	M	68	N	N	N	N	Y	CECT abdomen	1.4	1.5	NS			
102	699606	30	M	30	N	N	N	N	N	CECT abdomen	1.3	1.4	NS			
103	621071	45	F	64	N	N	N	N	N	CECT abdomen	1.3	1.2	NS			
104	997744	48	F	56	N	N	N	N	N	CECT abdomen	1.4	1.5	NS			
105	987879	30	M	61	N	N	N	N	N	CECT abdomen	1.5	1.4	NS			
106	224452	72	M	60	N	N	Y	N	N	CECT abdomen	1.4	1.3	NS			
107	839528	53	M	59	N	N	N	N	N	CECT KUB	1.3	1.4	NS			
108	381920	46	M	65	N	N	N	N	N	CECT abdomen	1.4	1.5	NS			
109	646760	80	F	56	N	N	Y	N	N	CECT neck	1.3	1.5	NS			
110	887247	50	F	57	N	N	N	N	N	CECT neck	1.4	1.5	NS			
111	497039	67	F	54	N	N	Y	N	N	CECT neck	1.3	1.4	NS			
112	231814	55	F	61	N	N	N	N	N	CECT neck	1.4	1.2	NS			
113	925723	42	M	67	N	N	N	N	Y	CECT neck	1.3	1.4	NS			
114	194880	60	M	72	N	N	N	N	Y	CECT neck	1.4	1.5	NS			
115	49711	49	M	74	N	N	N	N	Y	CECT neck	1.2	1.3	NS			

CE PA = contrast enhanced CT pulmonary angiogram, CECT = contrast enhanced computed tomography ,dL = deciliter, DM = diabetes mellitus, F = female, HTN = hypertension, kg = kilogram, KUB = kidney, ureter and bladder, M = male, mg = milligram, NAC = N acetyl cysteine, NS = not significant, NSAID = non-steroidal anti-inflammatory drugs, R = recovered, RI = renal insufficiency, S = significant

Sl. No	Trial ID	Age	Sex		Risk factor					Type of study	Serum creatinine (mg/dL)			Follow-up	Treatment	Outcome
				Body weight (in kg)	DM	HTN	Elderly	NSAID use	RI		Initial	At 48-72 hours	Change (S/NS)			
116	458196	35	F	68	N	N	N	N	Y	CECT neck	1.4	1.2	NS			
117	254150	35	F	71	N	N	N	N	Y	CECT neck	1.3	1.4	NS			
118	293227	65	F	60	N	N	N	N	N	CECT neck	1.4	1.4	NS			
119	401962	50	F	55	N	N	N	N	N	CECT neck	1.1	1.3	NS			
120	617458	75	M	49	N	N	Y	N	N	CECT neck	1.3	1.2	NS			
121	155	65	F	50	N	N	N	N	N	CECT neck	1.4	1.5	NS			
122	535026	65	F	59	N	N	N	N	N	CECT neck	1.2	1.4	NS			
123	565995	60	F	54	N	N	N	N	N	CECT neck	1.3	1.4	NS			
124	413902	85	M	57	N	N	Y	N	N	CECT neck	1.4	1.5	NS			
125	259659	70	F	62	N	N	Y	N	N	CECT neck	1.3	1.4	NS			
126	153672	32	M	65	N	N	N	N	N	CECT neck	1.3	1.5	NS			
127	941761	48	F	55	N	N	N	N	N	CECT neck	1.4	1.5	NS			
128	183197	80	M	47	N	Y	Y	N	N	CECT neck	1.3	1.4	NS			
129	307489	50	F	54	N	N	N	N	N	CECT neck	1.2	1.4	NS			
130	172492	32	F	59	N	N	N	N	N	CECT thorax	1.1	1.5	S	45	Hydration	R
131	588537	65	M	70	N	N	N	N	Y	CECT thorax	1.2	1.4	NS			
132	217333	35	M	68	N	N	N	N	Y	CECT thorax	1.3	1.4	NS			
133	598868	55	M	61	N	N	N	N	N	CECT thorax	1.2	1.4	NS			
134	961935	37	F	67	N	N	N	N	Y	CECT thorax	1.1	1.3	NS			
135	984179	50	M	72	N	N	N	N	Y	CECT thorax	1.4	1.4	NS			
136	594325	40	F	54	N	N	N	N	N	CECT thorax	1.3	1.4	NS			
137	148864	43	M	68	N	N	N	N	Y	CECT thorax	1.3	1.5	NS			
138	773018	22	M	54	N	N	N	N	N	CECT KUB	1.1	1.3	NS			
139	875115	18	M	49	N	N	N	N	N	CECT thorax	1.2	1.4	NS			
140	577762	60	M	75	N	Y	N	N	Y	CECT KUB	1.3	1.4	NS			
141	221641	48	M	57	N	N	N	N	N	CECT thorax	0.9	1	NS			
142	473233	60	F	58	N	N	N	N	N	CECT thorax	1.1	1.3	NS			
143	272520	59	M	57	N	N	N	N	N	CECT abdomen	1.1	1.2	NS			
144	738081	60	F	65	N	N	N	N	N	CECT abdomen	1.3	1.4	NS			
145	655440	87	M	52	N	N	Y	N	N	CECT abdomen	1.1	1.3	NS			
146	168843	27	M	74	N	N	N	N	Y	CECT abdomen	1.2	1.3	NS			
147	344031	26	F	67	N	N	N	N	Y	CECT KUB	1.3	1.4	NS			
148	194766	26	F	66	N	N	N	N	Y	CECT abdomen	1.1	1.3	NS			
149	615286	60	F	71	N	N	N	N	Y	CECT abdomen	1.2	1.4	NS			
150	242132	50	F	78	N	N	N	N	Y	CECT thorax	1.1	1.3	NS			
151	859925	75	M	70	N	N	Y	N	Y	CECT thorax	1.3	1.4	NS			
152	395126	65	M	50	N	N	N	N	N	CECT thorax	1.2	1.4	NS			
153	249046	42	F	68	N	N	N	N	Y	CECT thorax	1.1	1.4	S	45		R
154	668079	78	F	70	N	N	Y	N	Y	CE PA	1.2	1.4	NS			

CE PA = contrast enhanced CT pulmonary angiogram, CECT = contrast enhanced computed tomography ,dL = deciliter, DM = diabetes mellitus, F = female, HTN = hypertension, kg = kilogram, KUB = kidney, ureter and bladder, M = male, mg = milligram, NAC = N acetyl cysteine, NS = not significant, NSAID = non-steroidal anti-inflammatory drugs, R = recovered, RI = renal insufficiency, S = significant

Sl. No	Trial ID	Age	Sex	Risk factor						Type of study	Serum creatinine (mg/dL)			Follow-up	Treatment	Outcome
				Body weight (in kg)	DM	HTN	Elderly	NSAID use	RI		Initial	At 48-72 hours	Change (S/NS)			
155	835290	18	F	45	N	N	N	N	N	CECT Brain	1.1	1.2	NS			
156	708843	19	F	50	N	N	N	N	N	CECT Brain	1.2	1.3	NS			
157	932063	26	M	65	N	N	N	N	N	CECT KUB	1.2	1.3	NS			
158	96019	80	F	55	N	N	Y	N	N	CECT KUB	1.1	1.3	NS			
159	959373	55	F	70	N	N	N	N	Y	CECT neck	1.2	1.3	NS			
160	122376	85	M	64	N	N	Y	N	N	CECT neck	1.1	1.3	NS			
161	497907	85	F	60	N	N	Y	N	N	CECT neck	0.9	1.1	NS			
162	463798	70	F	51	N	N	Y	N	N	CECT neck	0.9	1	NS			
163	252985	60	F	64	N	Y	N	N	N	CECT neck	1.2	1.3	NS			
164	833037	40	M	75	N	Y	N	N	Y	CECT Brain	1.3	1.5	NS			
165	474499	35	M	81	N	N	N	N	Y	CECT abdomen	0.9	1.1	NS			
166	632186	45	F	76	N	N	N	N	Y	CECT abdomen	1.2	1.4	NS			
167	363282	75	M	60	N	Y	Y	N	N	CECT abdomen	1	1.3	S	45	Hydration	R
168	394711	37	M	83	N	N	N	N	Y	CECT Brain	1.1	1.2	NS			
169	781285	49	M	80	N	N	N	N	Y	CECT abdomen	0.9	1.1	NS			
170	386448	28	M	75	N	N	N	N	Y	CECT abdomen	1.1	1.2	NS			
171	815115	50	M	70	N	N	N	N	Y	CECT abdomen	0.9	1.1	NS			
172	481816	48	M	55	N	N	N	N	N	CECT thorax	1.1	1.3	NS			
173	739160	56	F	60	N	N	N	N	N	CECT abdomen	1.3	1.4	NS			
174	556223	70	M	75	N	Y	Y	N	Y	CECT Brain	1.2	1.4	NS			
175	959341	32	F	60	N	N	N	N	N	CECT KUB	1	1.1	NS			
176	402736	43	M	81	N	Y	N	N	Y	CECT thorax	1.2	1.5	S	45	Hydration /NAC	R
177	397158	70	F	60	N	N	Y	N	N	CECT thorax	1.1	1.3	NS			
178	692062	31	M	65	N	N	N	N	N	CECT thorax	0.9	1.1	NS			
179	672845	64	M	55	N	Y	N	N	N	CECT thorax	1.3	1.5	NS			
180	29080	43	M	60	N	N	N	N	N	CECT thorax	1.1	1.3	NS			
181	266327	42	F	62	N	N	N	N	N	CECT thorax	1.2	1.3	NS			
182	833220	65	F	64	N	Y	N	N	Y	CECT KUB	1	1.7	S	45	Hydration	R
183	985442	42	M	65	N	N	N	N	N	CECT neck	1.2	1.3	NS			
184	455305	68	M	55	N	N	Y	N	N	CECT neck	1.1	1.2	NS			
185	519168	65	M	60	N	N	N	N	N	CECT neck	1.3	1.4	NS			
186	899569	68	M	70	N	N	Y	N	Y	CECT neck	1.4	1.5	NS			
187	772831	48	F	60	N	N	N	N	N	CECT neck	1.1	1.2	NS			
188	240728	70	M	72	N	N	Y	N	Y	CECT neck	1.3	1.5	NS			
189	480745	41	M	60	N	N	N	N	N	CECT neck	1.1	1.2	NS			
190	314679	40	F	78	N	Y	N	N	Y	CECT thorax	0.8	0.9	NS			
191	992705	80	M	62	N	N	Y	N	N	CECT thorax	0.9	1.1	NS			
192	342879	56	F	60	N	N	N	N	N	CECT thorax	1.1	1.2	NS			
193	331829	65	F	55	N	N	N	N	N	CECT thorax	0.8	0.9	NS			

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Sl. No	Trial ID	Age	Sex	Risk factor						Type of study	Serum creatinine (mg/dL)			Follow-up	Treatment	Outcome
				Body weight (in kg)	DM	HTN	Elderly	NSAID use	RI		Initial	At 48-72 hours	Change (S/NS)			
194	369889	42	M	69	N	N	N	N	Y	CECT thorax	1	1.2	NS			
195	914989	70	F	55	N	N	Y	N	N	CECT thorax	1.2	1	NS			
196	367603	38	M	76	N	N	N	N	Y	CECT Brain	0.9	0	NS			
197	971886	26	M	70	N	N	N	N	Y	CECT Brain	1.1	1.1	NS			
198	711038	75	M	60	N	N	Y	N	N	CECT Brain	1.2	1.3	NS			
199	947298	19	M	52	N	N	N	N	N	CECT Brain	1.1	1.1	NS			
200	653773	70	F	55	N	N	Y	N	N	CECT Brain	1.3	1.5	NS			
201	613591	22	M	60	N	N	N	Y	N	CECT abdomen	1.1	1.2	NS			
202	786051	65	M	55	N	N	N	N	N	CECT abdomen	1.2	1.4	NS			
203	218405	45	M	73	N	N	N	N	Y	CECT abdomen	0.8	0.9	NS			
204	557454	30	F	66	N	N	N	N	Y	CECT abdomen	1	1.2	NS			
205	187180	25	M	72	N	N	N	N	Y	CECT abdomen	1.2	1.1	NS			
206	805693	70	F	60	N	N	Y	N	N	CECT abdomen	1.2	1.3	NS			
207	340563	40	F	70	N	N	N	N	Y	CECT abdomen	1.1	1.3	NS			
208	264515	28	F	60	N	N	N	N	N	CECT abdomen	1.2	1.3	NS			
209	313197	33	M	70	N	N	N	N	Y	CECT abdomen	1.1	1.2	NS			
210	977960	45	M	63	N	Y	N	N	N	CECT thorax	1.2	1.5	S	45	Hydration	R
211	789346	64	M	70	N	N	N	N	Y	CECT thorax	1.1	1.3	NS			
212	690327	43	M	74	N	N	N	N	Y	CECT neck	1	1.2	NS			
213	756354	46	F	63	N	N	N	N	N	CECT neck	1.2	1.3	NS			
214	160533	68	M	60	N	N	Y	N	N	CECT neck	0.8	0.9	NS			
215	919751	32	M	56	N	N	N	N	N	CECT neck	1.1	1.3	NS			
216	182680	60	M	62	N	N	N	N	N	CECT neck	0.9	1	NS			
217	375214	60	F	55	N	N	N	N	N	CECT neck	1.1	1.3	NS			
218	195132	70	M	60	N	N	Y	N	N	CECT neck	1	1.2	NS			
219	559002	40	M	70	N	N	N	N	Y	CECT neck	0.9	1.1	NS			
220	439271	38	M	70	N	N	N	N	Y	CECT KUB	1.1	1.3	NS			
221	887338	29	M	65	N	N	N	N	N	CECT KUB	1.2	1.2	NS			
222	466684	80	M	55	N	N	Y	N	N	CECT Brain	1.1	1.3	NS			
223	714159	20	M	50	N	N	N	N	N	CECT Brain	0.9	1	NS			
224	158193	70	F	60	N	N	Y	N	N	CECT abdomen	1.1	1.3	NS			
225	894252	45	F	65	N	N	N	N	N	CECT thorax	0.9	1.1	NS			
226	37581	65	F	60	N	Y	N	N	N	CECT Brain	0.9	1.1	NS			
227	565132	65	F	58	N	N	N	N	N	CECT abdomen	1.2	1.2	NS			
228	882284	40	M	78	N	N	N	N	Y	CECT abdomen	1.1	1.3	NS			
229	218906	48	F	58	N	N	N	N	N	CECT abdomen	1	1.2	NS			
230	813610	58	M	65	N	N	N	N	N	CECT abdomen	1.1	1.3	NS			
231	188893	56	M	70	N	Y	N	N	Y	CECT abdomen	1.2	1.3	NS			
232	344696	50	F	68	N	N	N	N	Y	CECT abdomen	1.1	1.2	NS			

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				Body weight (in kg)	DM	HTN	Elderly	NSAID use	RI		Initial	At 48-72 hours	Change (S/NS)			
233	613178	45	M	75	N	N	N	N	Y	CECT abdomen	0.9	1.1	NS			
234	673811	66	F	60	N	N	Y	N	N	CECT abdomen	1	1.1	NS			
235	86825	50	M	70	N	N	N	N	Y	CECT KUB	1.1	1.2	NS			
236	77089	32	M	60	N	N	N	N	N	CECT KUB	1.2	1.2	NS			
237	605184	50	M	65	N	N	N	N	N	CECT neck	1	1.1	NS			
238	215795	54	F	55	N	N	N	N	N	CECT neck	0.9	1	NS			
239	604854	68	F	60	N	N	Y	N	N	CECT neck	1.2	1.3	NS			
240	529041	70	M	58	N	N	Y	N	N	CECT neck	1	1.2	NS			
241	102460	64	F	55	N	N	N	N	N	CECT neck	1.1	1.3	NS			
242	15932	60	F	58	N	N	N	N	N	CECT neck	1	1.1	NS			
243	632773	65	F	50	N	N	N	N	N	CECT neck	1.2	1.3	NS			
244	698616	46	M	60	N	N	N	N	N	CECT neck	1	1.1	NS			
245	686303	86	M	60	N	N	Y	N	N	CECT thorax	1	1.4	S	45	Hydration	R
246	976526	40	F	75	N	N	N	N	Y	CECT thorax	1.1	1.2	NS			
247	859023	65	F	60	N	N	N	N	N	CECT thorax	1	1.2	NS			
248	699086	45	F	65	N	N	N	N	N	CECT thorax	1.1	1.3	NS			
249	686390	50	M	70	N	N	N	N	Y	CECT thorax	1	1.2	NS			
250	56440	33	F	60	N	N	N	N	N	CE PA	1.1	1.3	NS			
251	776245	52	M	82	N	N	N	N	Y	CECT thorax	1.2	1.4	NS			
252	713597	70	F	56	N	N	Y	N	N	CECT abdomen	1.2	1.3	NS			
253	194532	53	F	65	N	N	N	N	N	CECT abdomen	0.9	1.1	NS			
254	265086	60	M	70	N	N	N	N	Y	CECT abdomen	1.1	1.2	NS			
255	744072	68	F	59	N	N	Y	N	N	CECT abdomen	1	1.2	NS			
256	597912	22	M	60	N	N	N	N	N	CECT abdomen	1	1.2	NS			
257	924869	59	M	65	N	N	N	N	N	CECT abdomen	1.2	1.2	NS			
258	807524	70	M	60	N	N	Y	N	N	CECT abdomen	1.1	1.3	NS			
259	178448	55	M	75	N	Y	N	N	Y	CECT abdomen	1	1.2	NS			
260	39124	45	M	82	N	N	N	N	Y	CECT Brain	1.1	1.2	NS			
261	849402	40	M	70	N	N	N	N	Y	CECT Brain	1	1.2	NS			
262	310525	65	M	65	N	N	N	N	N	CECT Brain	1.1	1	NS			
263	923700	60	F	78	N	N	N	N	Y	CECT thorax	1.2	1.3	NS			
264	304806	30	F	65	N	N	N	N	N	CECT thorax	1	1.1	NS			
265	745459	58	F	60	N	N	N	N	N	CECT thorax	1.2	1.1	NS			
266	109033	55	F	58	N	N	N	N	N	CECT thorax	1.3	1.4	NS			
267	742900	60	M	60	N	N	N	N	N	CECT thorax	1.2	1.3	NS			
268	514136	46	F	65	N	N	N	N	N	CECT abdomen	1.3	1.4	NS			
269	340841	45	F	60	N	N	N	N	N	CECT abdomen	0.9	1.1	NS			
270	793818	32	M	72	N	N	N	N	Y	CECT abdomen	1.1	1.3	NS			
271	678116	60	M	65	N	N	N	N	N	CECT abdomen	0.9	1.2	S	45	Hydration	R

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				Body weight (in kg)	DM	HTN	Elderly	NSAID use	RI		Initial	At 48-72 hours	Change (S/NS)			
272	827303	65	F	52	N	N	N	N	N	CECT neck	1.1	1.3	NS			
273	996652	58	F	55	N	N	N	N	N	CECT neck	1.4	1.5	NS			
274	951888	60	F	60	N	N	N	N	N	CECT KUB	1.2	1.13	NS			
275	816583	70	M	75	N	N	Y	N	Y	CECT thorax	1	1.2	NS			
276	522806	80	M	60	Y	N	Y	N	N	CECT abdomen	1	1.2	NS			
277	726094	68	F	67	N	N	Y	N	Y	CE PA	1.2	1.3	NS			
278	269077	55	F	63	N	N	N	N	N	CECT abdomen	0.9	1.1	NS			
279	819671	55	F	64	N	N	N	N	N	CECT Brain	1.2	1.3	NS			
280	249437	65	F	72	N	N	N	N	Y	CECT abdomen	1	1.2	NS			
281	263218	50	F	62	N	N	N	N	N	CECT abdomen	1	1.2	NS			
282	170154	45	F	69	N	N	N	N	Y	CECT abdomen	1.1	1.3	NS			
283	718574	65	F	70	N	N	N	N	Y	CECT thorax	1.2	1.3	NS			
284	889469	82	F	55	Y	N	Y	N	N	CECT KUB	1.4	1.5	NS			
285	315573	55	F	71	N	N	N	N	Y	CECT KUB	1.2	1.4	NS			
286	496615	64	M	67	N	N	N	N	Y	CECT KUB	0.9	1.1	NS			
287	866540	67	M	60	N	N	Y	N	N	CECT KUB	1.3	1.2	NS			
288	727177	60	F	70	N	N	N	N	Y	CECT KUB	1.1	1.7	S	45	Hydration /NAC	R
289	158893	55	M	65	N	Y	N	N	Y	CECT KUB	1.3	1.7	S	45	Hydration	R
290	673055	88	F	50	N	Y	Y	N	N	CECT neck	1.2	1.4	NS			
291	661333	38	F	70	N	N	N	N	Y	CECT Brain	1.1	1.2	NS			
292	424602	37	M	72	N	N	N	N	Y	CECT Brain	1	1.1	NS			
293	327821	32	F	58	N	N	N	N	N	CECT Brain	1.1	1.2	NS			
294	707560	56	M	60	N	N	N	N	N	CECT Brain	1.3	1.4	NS			
295	670711	70	M	62	N	N	Y	N	N	CECT Brain	1	1.2	NS			
296	595017	75	M	62	N	Y	Y	N	N	CECT abdomen	1.2	1.3	NS			
297	901136	45	F	60	N	N	N	N	N	CECT abdomen	1.4	1.5	NS			
298	443127	27	F	58	N	N	N	N	N	CECT KUB	1.1	1.2	NS			
299	707429	30	M	65	N	N	N	N	N	CECT abdomen	0.8	0.9	NS			
300	132797	66	F	58	N	N	Y	N	N	CECT abdomen	1.1	1.2	NS			
301	775922	48	F	60	N	N	N	N	N	CECT abdomen	0.9	1	NS			
302	954620	65	F	55	N	N	N	N	N	CECT abdomen	1	1.1	NS			
303	148099	47	M	65	N	N	N	N	N	CECT neck	0.8	0.9	NS			
304	525935	55	M	60	N	N	N	N	N	CECT neck	1	1.1	NS			
305	301937	70	M	60	Y	N	Y	N	N	CECT KUB	1	1.2	NS			
306	941316	33	M	65	N	N	N	N	N	CECT abdomen	0.8	0.9	NS			
307	1433	36	M	60	N	N	N	N	N	CECT abdomen	1	1.1	NS			
308	216127	56	M	70	Y	N	N	N	Y	CECT thorax	1.1	1.2	NS			
309	934091	65	M	60	Y	Y	N	N	N	CECT thorax	1.2	1.4	NS			
310	61644	50	M	70	Y	N	N	N	Y	CECT abdomen	1.1	1.2	NS			

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