The aim of the present paper is to discuss some strategies to minimize contrast medium (CM) doses in patients at risk of CM-induced nephropathy (CIN). It will concentrate on computed tomographic angiography (CTA) but also includes some CM-sparing techniques for percutaneous catheter angiography (PCA) and vascular interventions (PVI).

Manner of CM administration

The CIN literature is largely based on intraarterial (i.a.) administration of CM, above all coronary angiography and interventional procedures, with an overall incidence of 1–2% [1]. The presence of multiple CIN risk factors or high-risk clinical scenarios may create a high risk for CIN (=50%) and acute renal failure (=15%) requiring dialysis [2, 3].

Established risk factors include renal impairment, diabetic nephropathy, congestive heart failure, hypotension, dehydration, low serum albumin levels, anemia, hypoxic conditions, NSAID, nephrotoxic antibiotics/cytostatics, and high contrast medium doses [1]. Features classifying a patient at high risk of CIN may include a GFR <40–45 ml/min or multiple risk factors [4].

The incidence of CIN following CM-enhanced CT is not well documented. It has also been argued that the apparently lower risk of CIN associated with intravenous (i.v.) CM administration [5, 6, 7], the lack of controlled i.v.CM studies [7, 8], and serum creatinine variations of other causes than CIN [9] may “make it defensible to consider using CM even in patients with greater levels of background risk factors (e.g., greater degrees of preexisting chronic renal insufficiency) than one would be comfortable with in the intraarterial setting” [6], and that “international radiologic professional organizations should revisit the basis of their practice guidelines to reduce their implications about the danger of CIN with CM-enhanced CT” [7].

However, in the relatively few published reports of CIN following CM-enhanced CT the incidence may vary between 0 and 42%, depending on definitions, degree of renal impairment, and number and degree of risk factors [7, 10, 11, 12, 13]. In one controlled study with critically ill patients but normal serum creatinine, 19% of the patients undergoing CM-enhanced CT had a creatinine rise >25% from baseline compared with only 1% in the matched control group not receiving CM. Hemodialysis was required by 3% of patients in the CT group.

In a recent prospective study of unselected emergency patients, all receiving 120 ml of a 370 mg I/ml solution (44 g iodine), 11% (n=70/633) increased their serum creatinine ≥44 μmol/l or ≥25% of whom 9% (n=6) developed CM-induced severe renal failure, which contributed to death in 4 of the 6 patients [14]. It should also be noted that in randomized studies comparing renal effects of various CM, high-risk patients (e.g., unstable renal function, heart failure, uncontrolled diabetes, recent CM examinations) are often excluded [12, 15, 16, 17]. This bias in patient selection compared with coronary studies, where high-risk patients can not be excluded from life-saving procedures, may in part explain the illusive opinion that i.v. CM injection implies a lesser risk of CIN than i.a. administration. Furthermore, there is not one single study comparing the risk of i.v. versus i.a. injections in patients with matched risk factors receiving the same amount of CM.

Intravenous CM administration not proven less nephrotoxic than intraarterial administration

It must also be recognized that coronary CM injections, e.g., injections into carotid, subclavian, mesenteric, distal aortic, and iliacofemoral arteries are in fact intravenous relative to the kidneys, since the CM has to pass the capillary beds and veins to the right atrium and pulmonary circulation before reaching the kidneys as in CT. A recent study of CIN showed that i.v. CM injections were actually associated with a higher mortality risk than i.a. ad-
ministration [18]. One explanation may be that the entire CM dose in CT is injected within 1 minute and, thus, may strike the kidneys at a considerable higher dose rate compared with a coronary arterial procedure that may last for 15–60 min or even longer. Animal studies also indicate that acute i.v. toxicity of CM is very dependent on the rate of injection [19]. Thus, it may seem premature to consider the risk of CIN less following i.v. injections than after i.a. administration. However, it should be recognized that supra- and juxtarenal aortic as well as selective renal injections should impose a greater risk of CIN, presumably because of higher concentrations of CM reaching the kidneys and also exerting hypertonic effects if plasma hypertonic CM are used.

Prophylaxis

A number of prophylactic regimen studies have been performed and meta-analyzed [20]. So far no adjunctive medical pharmacological treatment has convincingly been proved to be efficacious in reducing the risk of CIN [21], including acetylcycteine [22] and hydration with sodium bicarbonate instead of saline [23]. Hemodilution is ineffective and hemofiltration is impractical in clinical routine [21]. Thus, treating modifiable risk factors [1] and instituting adequate intravenous volume expansion with isotonic crystalloid solutions [21] are two of the three corner stones to minimize the risk of CIN. The third is to reduce the dose of the offending agent itself, i.e., the contrast medium [5].

### Evaluation of renal function

It is well recognized that serum creatinine is a poor predictor of renal function [24], especially in elderly with decreasing muscle mass, the major source of creatinine. In one study, 50% of patients ≥70 years with a normal serum creatinine had a glomular filtration rate (GFR) ≤50 ml/min [25].

- **Use estimated GFR, not serum creatinine alone, to evaluate renal function**

Measurement of GFR is regarded the best index of the level of renal function in healthy and diseased patients [26], but is work-intensive, relatively expensive and time-consuming, and therefore unsuitable in clinical practice prior to CM administration. Instead, GFR should be estimated (eGFR) taking account not only serum creatinine but also anthropometric (weight and height) and/or demographic (gender and age) data as a measure of muscle mass by using dedicated GFR prediction equations [27], e.g., the Cockcroft-Gault [28], MDRD [29], CKD-EPI [30], and Lund-Malmö equations [31]. Consequently, newly developed CIN risk scores for coronary artery interventions also include eGFR [32, 33]. Before adapting a GFR prediction equation, the following should be considered:

- the creatinine assay in the local laboratory must be calibrated according to the specific method used in the laboratory where the equation was developed [34],
- dosing of drugs excreted by glomerular filtration should be based on GFR not adjusted for body surface area (absolute GFR; ml/min). GFR adjusted to body surface area (relative GFR; ml/min/1.73 m²) will overestimate the actual GFR in small patients, especially children, and underestimate the GFR in large individuals (http://www.kidney.org/professionals/klspdf/KBA_FAQs_AboutGFR.pdf). Tab. 1). MDRD and CKD-EPI primarily give relative GFR, which can be converted to absolute GFR using a body surface area equation, e.g., the commonly used Dubois formula [35]: area (m²) = weight0.425×height0.725×0.007184, weight in kg and height in cm, and  
- estimated GFR is only within 30% of measured GFR in 80–85% of the patients [30, 31]. Thus, a patient with eGFR of 50 ml/min may actually only have a real GFR of 35 ml/min.

### Systemic drug exposure and CIN

**AUC**

Following injection of CM, blood samples may be used to calculate the area under the plasma concentration–time curve (AUC). It is directly proportional to CM dose and inversely correlated with GFR. AUC is a fundamental pharmacokinetic parameter used to estimate systemic exposure of drugs that are distributed and eliminated according to linear kinetics, e.g., contrast media [36, 37]. The systemic exposure of such a drug is often well correlated with its toxicity and, hence, is generally held as an index for dose optimization [36]. The clinical value of AUC as a predictor of nephrotoxicity has been shown for a variety of drugs and, thus, the CM dose/GFR ratio may be used as a potential indicator of the risk for CIN [37].

**Gram-iodine/eGFR ratio**

CM doses in CIN risk scores and recommendations to minimize the risk of CIN have for obscure reasons often been based only on volumes [5, 32, 33]. It should be expressed in terms of gram iodine (g-I), since concentrations of commercially available CM varies from 140–400 mg I/ml. This also makes it easier to compare...
CM doses and expand the experience of CIN made from one examination or department to another if different concentrations are used. Furthermore, common g-I doses for radiography-based procedures, i.e., 10–90 g-I, are in the same numerical range as patients' GFR, i.e., 10–90 ml/min. Thus, forming a g-I/eGFR ratio combines CM volume and concentration, serum creatinine, age, and body size into a single continuous risk variable and provides the examiner with a simple numerical relationship and an expedient way to predict the risk of CIN.

Gram-iodine/eGFR ratio a significant independent predictor of CIN

Mounting evidence from coronary interventions indicates that a g-I/eGFR ratio <1.0 is associated with a low risk of CIN, especially in the absence of multiple risk factors [38, 39, 40, 41, 42, 43]. Individual patient data from CT studies are lacking, but weighted mean data from CT studies show an 8% incidence of CIN at a g-I/eGFR ratio of 0.9 (Table 2), indicating that the ratio should also be kept <1.0 for CT. If a CM-based examination is deemed necessary in a high-risk patient, the author recommends keeping the g-I/eGFR ratio as low as reasonably achievable, i.e., below 0.5.

Contrast media dosing in CTA

Iodine CM are distributed in the extracellular fluid space, i.e., plasma and extravascular interstitium [44, 45], which is related to body weight (BW) [46, 47, 48, 49]. The distribution volume of CM has been calculated to about 0.25 l/kg in human volunteers [46, 48] and CM injection protocols tailored to patient weight have been shown to reduce interindividual differences of CM enhancement [50, 51, 52, 53, 54, 55].

Volume distribution of CM is related to body weight

It can be anticipated that non-BW standardized CM doses have been adjusted to provide proper enhancement in larger patients. Thus, dosing per kg BW im-

Abstract · Zusammenfassung

U. Nyman
Minimizing contrast-induced nephropathy. Strategies in CTA, catheter angiography and interventions

Abstract

The aim of the present paper is to discuss strategies to minimize contrast medium (CM) doses in patients at risk of CM-induced nephropathy (CIN) after computed tomographic angiography (CTA), and percutaneous catheter angiography (PCA) and vascular interventions (PVI). In general a gram-iodine (g-I)/eGFR ratio ≥1.0 appears to be a significant and independent predictor of CIN in CTA and coronary interventions. In high CIN-risk patients (e.g., eGFR <45 ml/min or multiple risk factors), it is recommended to keep the g-I/eGFR ratio <0.5. In azotemic patients, 80 kVp CTA may be accomplished with 100–150 mg I/kg while x-ray tube loading must be increased to maintain the contrast-to-noise ratio at an acceptable level. Peripheral PCA/PVI based on digital subtraction technique may be performed with 75–150 mg I/ml, or even lower if the equipment permits manual setting of the x-ray tube potential. Coronary arteriography/ interventions may be achieved with 140–150 mg I/ml, i.e., less than half the routinely used concentrations (~320–370 mg I/ml), especially in thinner patients with increased iodine attenuation due to automatic down regulation of the x-ray tube potential.

The English full-text version of this article is available at SpringerLink (under "Supplemental").

Keywords
Angiography · Acute kidney injury · Computed tomography · Contrast media · Renal insufficiency

Minimierung kontrastmittelinduzierter Nephropathien. Strategien bei CTA, Katheterangiographie und Interventionen

Zusammenfassung

Ziel der vorliegenden Arbeit ist die Diskussion von Strategien zur Minimierung der Kontrastmittel(KM)-Dosen bei Patienten mit dem Risiko einer KM-induzierten Nephropathie („contrast medium-induced nephropathy“, CIN) nach Computertomographie(CT)-Angiographie, perkutaner Katheterangiographie (PCA) und vaskulärer Intervention (PVI). Allgemein scheint ein Verhältnis zwischen der Jodmenge in Gramm und der geschätzten glomerulären Filtrationsrate (g-I/eGFR) ≥1,0 ein signifikanter und unabhängiger Prädiktor einer CIN bei CTA und Coronarinterventionen zu sein. Bei Patienten mit hohem CIN-Risiko (z. B. eGFR <45 ml/min oder multiple Risikofaktoren) wird empfohlen, die g-I/eGFR-Ratio <0,5 zu halten. Bei Patienten mit Azotämie kann eine 80-kVp-CTA mit 100–150 mg I/kg durchgeführt werden, dabei muss die Leistung der Röntgenröhre erhöht werden, um den Kontrast-Rausch-Abstand auf einem akzeptablen Niveau zu halten. Eine periphere PCA/PVI auf der Basis der digitalen Subtraktionstechnik kann mit 75–150 mg I/ml erfolgen oder auch weniger, wenn das Gerät die manuelle Einstellung des Röntgenröhrenpotenzials erlaubt. Koronarangiographien/-interventionen können bei 140–150 mg I/ml erfolgen, d. h. mit weniger als der Hälfte der üblicherweise verwendeten Konzentrationen (~320–370 mg I/ml), vor allem bei dünnen Patienten mit erhöhter Jodabschwächung aufgrund der automatischen Herabregulierung des Röntgenröhrenpotenzials.

Die englische Volltextversion dieses Beitrags ist über SpringerLink (unter “Supplemental”) verfügbar.

Schlüsselwörter
Angiographie · Akutes Nierenversagen · Computertomographie · Kontrastmittel · Niereninsuffizienz
Tab. 2  Literature review of nonrandomized and randomized CT studies from 2000–2008

<table>
<thead>
<tr>
<th>First author</th>
<th>Type of CM</th>
<th>n</th>
<th>CM dose (gram iodine)</th>
<th>eGFR (ml/min)</th>
<th>g-l/eGFR ratio</th>
<th>CIN (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tepe² [10]</td>
<td>LOCM</td>
<td>42</td>
<td>23</td>
<td>34</td>
<td>0.7</td>
<td>21</td>
</tr>
<tr>
<td>Luft [79]</td>
<td>LOCM</td>
<td>33</td>
<td>49</td>
<td>63</td>
<td>0.8</td>
<td>9.1</td>
</tr>
<tr>
<td>Kolehmainen [80]</td>
<td>LOCM/IOCM</td>
<td>50</td>
<td>35</td>
<td>29</td>
<td>1.2</td>
<td>16</td>
</tr>
<tr>
<td>Garcia-Ruiz [81]</td>
<td>LOCM</td>
<td>50</td>
<td>48</td>
<td>30</td>
<td>1.6</td>
<td>4.0</td>
</tr>
<tr>
<td>Becker [82]</td>
<td>LOCM</td>
<td>100</td>
<td>27</td>
<td>41</td>
<td>0.7</td>
<td>9.0</td>
</tr>
<tr>
<td>Barrett [15]</td>
<td>LOCM/IOCM</td>
<td>150</td>
<td>40</td>
<td>45</td>
<td>1.0</td>
<td>3.9</td>
</tr>
<tr>
<td>Thomsen² [17]</td>
<td>LOCM/IOCM</td>
<td>148</td>
<td>40</td>
<td>42</td>
<td>1.0</td>
<td>6.1</td>
</tr>
<tr>
<td>Nguyen [12]</td>
<td>LOCM</td>
<td>56</td>
<td>37</td>
<td>53</td>
<td>0.7</td>
<td>28</td>
</tr>
<tr>
<td>Kuhn [16]</td>
<td>LOCM/IOCM</td>
<td>248</td>
<td>36</td>
<td>49</td>
<td>0.7</td>
<td>5.2</td>
</tr>
<tr>
<td>Weisbord [83]</td>
<td>LOCM</td>
<td>421</td>
<td>48</td>
<td>53</td>
<td>0.9</td>
<td>6.5</td>
</tr>
</tbody>
</table>

Weighted mean data 1,301 40 47 0.9 7.8

² Reporting gram-iodine (g-I) dose, estimated glomerular filtration rate (eGFR), and incidence of contrast medium (CM)-induced nephropathy (CIN; serum creatinine rise ≥25% or ≥44 μmol/l above baseline). Only results for low-osmolar contrast media (LOCM) were included unless there was no significant difference between LOCM and IOCM (iso-osmolar contrast media). Mean g-I dose, mean eGFR, g-I/eGFR ratio (calculated by the author from the mean values), incidence of CIN in each study are given. Weighted mean value with individual study sizes as weights were finally calculated. The weighted mean of the g-I/eGFR ratio was based on log-transformation. Only control group not receiving acetylcysteine included. Based on individual data in the report.

Tab. 3  Individualization of contrast medium dose a

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Elderly woman</th>
<th>Young male</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>80</td>
<td>50</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Serum creatinine (μmol/l)</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Estimated GFR (ml/min) [28]</td>
<td>31</td>
<td>135</td>
</tr>
<tr>
<td>CM volume of distribution (0.25 l/kg) [48]</td>
<td>12.5</td>
<td>25</td>
</tr>
<tr>
<td>Blood volume (0.07 l/kg) [49]</td>
<td>3.5</td>
<td>7.0</td>
</tr>
<tr>
<td>CM dose per kg (mg I/kg) at a fixed dose 125 ml 320 mg I/ml=40 g-I</td>
<td>800</td>
<td>400</td>
</tr>
<tr>
<td>CM dose 400 mg I/kg (grams iodine)</td>
<td>20</td>
<td>40</td>
</tr>
<tr>
<td>Dose rate (mg I/kg/s) at 4 ml/s (400 mg I/kg)</td>
<td>26</td>
<td>13</td>
</tr>
<tr>
<td>Dose rate (mg I/kg/s) at fixed injection time 16 s (400 mg I/kg)</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>Cardiac output anticipated (l/min)</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Dose rate (mg I/kg/s) adapted to cardiac output by changing the dose/kg:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- 250 mg I/kg in 16 s</td>
<td>16</td>
<td>31</td>
</tr>
<tr>
<td>- 500 mg I/kg in 16 s</td>
<td>12.5</td>
<td>50</td>
</tr>
<tr>
<td>Resulting CM dose (grams iodine) when using 80 instead of 120 kVp due to low eGFR; 250 → 150 mg I/kg (factor 1.6)</td>
<td>7.5</td>
<td></td>
</tr>
<tr>
<td>g-I/eGFR ratio (ml/min)</td>
<td>0.24</td>
<td>0.37</td>
</tr>
</tbody>
</table>

a Individualizing contrast medium (CM) dose in an azetemic elderly patient with low weight and reduced cardiac output (CO); and a younger patient with high weight, increased cardiac output, and normal renal function during CT angiography by dosing per kg body weight, applying fixed injection duration, considering differences in cardiac output, and decreasing x-ray tube potential in the elderly azetemic patient. The younger healthy person may need 50 gram-iodine (g-I) while the elderly may do diagnostically well with only 7.5 g-I resulting in a g-I/eGFR ratio of only 0.24 at an eGFR of 31 ml/min.

extracellular volume, i.e., the distribution volume of CM [47, 56].

When performing CTA, dosing per kg BW should be combined with a fixed injection duration adapted to scan time to provide for a constant influx of iodine atoms per kg (relates to plasma volume) per second and an arterial enhancement unrelated to body weight [51, 54, 55]. Otherwise CM-enhancement for a “low-weight” patient may become considerably higher than for a “high-weight” patient and even too high for diagnostic requirements with an unnecessary risk of CIN. Calculation of individual CM volumes and injection rates based on dose/kg, concentration, and injection duration can be easily performed with a Microsoft Excel spreadsheet or using a dedicated computer program developed to calculate both eGFR and CM injection parameters from predefined CT protocols (OmniVis, GE Healthcare, Stockholm, Sweden).

Dosing per kg at fixed injection duration in CTA gives a constant influx of iodine atoms/kg/s

A maximum dose weight of about 80–90 kg may be chosen, assuming that higher weight in most patients corresponds to fatty tissue, which contributes minimal additional mass in most patients. In fact, CM doses regarded sufficient for 80–100 kg patients could be halved for 40–50 kg patients to obtain the same degree of enhancement. A maximum dosing weight of, e.g., 80–90 kg should also be chosen, assuming that higher weights in most patients correspond to adipose tissue with minimal contribution to the
that the choice of CM concentration is of no concern regarding CM enhancement when these principles are used [57, 58].

X-ray tube potential

Iodine attenuation of photons is highly dependent on the x-ray spectra used. As an example decreasing the x-ray tube peak kilovoltage (kVp) from the commonly used 120 kVp for CTA to 80 kVp brings the x-ray spectra closer to the k-edge of iodine (33.2 keV) and increases the attenuation of iodine by a factor of 1.6 [59]. Thus, the CM dose may be reduced by a factor of 1.6 while maintaining the attenuation at the same level as that obtained at 120 kVp.

Decreasing X-ray tube potential increases iodine attenuation

At the same time x-ray tube loading in terms of milliampere seconds (mAs) has to be increased by a factor of four to keep image noise constant, resulting in a 50% increase in radiation dose for the same reference object [54, 55]. Thus, the diagnostic quality in terms of contrast-to-noise ratio (CNR) may be preserved. It may require 300–400 effective mAs in the thorax and 500–600 effective mAs in the abdomen. The increased radiation dose seems to be of less importance in elderly azotemic patients than the risk of CIN [54, 55].

Cardiac output and CM enhancement

Cardiac output has a major influence on vascular CM enhancement in CTA. Enhancement increases with decreasing cardiac output due to less dispersion of the CM bolus as well as slower inflow of unenhanced blood to the superior vena cava (from the jugular and contralateral brachiocephalic veins) and right atrium (from inferior vena cava) with less dilution of the bolus [60, 61].

Renal impairment may induce cardiac dysfunction and vice versa, the s.c. cardio-renal syndrome [62]. Since increasing age also predisposes to decreasing renal function and cardiac diseases, many azotemic patients will have reduced cardiac output, an additional CIN risk factor [1]. Thus, it would be possible to decrease CM dose in most azotemic patients for the same vascular CM-enhancement as that obtained in patients with normal cardiac function. At the same time, prophylactic hydration to avoid CIN in patients with poor cardiac function is a problem, which is why reduction of CM dose may offer the best protection against CIN, while preserving diagnostic quality. Thus, in high-risk patients it may be warranted to ask for an echocardiogram or to use a handheld electrical velocimeter (Icon*, Osypka Medical, Berlin, Germany) in the CT suite to evaluate cardiac output prior to a CTA [61].

How the individual CM doses may vary during CTA when combining the above mentioned parameters, i.e., dosing per kg body weight, applying a fixed injection duration, considering cardiac output, and decreasing x-ray tube potential in the elderly azotemic patient, is shown in Tab. 3.

CTA in azotemic patients

In a survey of routine 16-multirow detector CT (MDCT) protocols to diagnose pulmonary embolism (PE), CM doses ranged from 28–55 g-I. By combining CM dose tailored to BW, a fixed injection time adapted to scan time, automatic bolus tracking, saline chaser, x-ray tube potential of 80 kVp, and anticipating a decreased cardiac output in azotemic patients, it has been possible to halve the CM dose from 300 at 120 kVp and to 150 mg I/kg at 80 kVp or to a median total dose of 10 g-I when performing pulmonary CTA in azotemic patients [55]. Arterial attenuation, image noise, and CNR were similar to that obtained with 24–42 g-I at 120–
Infobox 1  Precautions and techniques to save contrast media in CT angiography of azotemic patients
- If possible, delay examination, treat risk factors, and institute hydration
- Use noncontrast-enhanced CT to confirm or exclude ruptured aortic aneurysms; be prepared to perform CM-enhanced CT if rupture diagnosed and endovascular repair is an option
- Dose per kg body weight
- Use fixed injection duration adapted to scan time
- Halve the contrast medium dose by:
  - reducing x-ray tube potential to 80 kVp and increase mAs to keep image noise at an acceptable level [55] and
  - considering decreased cardiac output in elderly, azotemic, and cardiac patients
- Consider iodine-CM doses iso-attenuating with gadolinium-CM (see Tab. 4)
- Use “saline chaser” to make use of the CM that otherwise would be temporarily trapped in the arm veins at the end of injection

Infobox 2  Precautions and techniques to save contrast media during catheter angiography and interventions in azotemic patients
- If possible, delay examination, treat risk factors, and institute hydration
- Substitute echocardiography for left ventriculography
- Map vascular anatomy/pathology as far as possible without CM procedures, for example:
  - Doppler ultrasound or use non-CM enhanced MR angiography sequences, and
  - CT to map major renal artery origins to define optimal angiographic projections for profiling their origin or to guide selective catheterization for pressure measurements
- Stage diagnostic and therapeutic procedures
- Use biplane technique
- Replace test injections with a diagnostic DSA run (digital subtraction angiography)
- Scrutinize each series to avoid unnecessary standard projections
- Substitute manometry of query stenosis for multiple projections
- Counteract the dilution effect of high aortic blood flow by digital compression of CFA or bilateral thigh tourniquets according to Fariñas [84]
- Direct contrast medium by occluding “healthy vessels”
- Use carbon dioxide in infradiaphragmatic aorta and arteries, and in venous studies [77] supplemented with small doses of iodine-CM when necessary
- Consider iodine-CM iso-attenuating with gadolinium-CM [76]
- Decrease x-ray tube potential, if possible, to permit lower iodine concentrations
- Plasma isotonic CM for aortorenal angiography
- Perform selective and superselective “single leg run-off” with focus on the symptomatic leg only, preferably with stepping technique and primary selection of the most optimal view:
  - contralateral arterial aneurysm for the iliac bifurcation,
  - ipsilateral arterial aneurysm for common femoral artery bifurcation,
  - ipsilateral arterial aneurysm for popliteal trifurcation, and
  - lateral view of the foot
- Use abdominal compression devices to permit lower x-ray tube potential and limit patient movements

140 kVp [54, 63, 64]. The median g-I/eGFR ratio was 0.3 and no CIN episodes were recorded. These principles have also been adopted in the author’s clinical routine for CT angiography of aortoiliac, renal, and mesenteric arteries (Fig. 1).

Ultra-low iodine doses

Before the advent of nephrogenic systemic fibrosis (NSF), gadolinium CM (Gd-CM) was enthusiastically used for CTA [65, 66] and PCA/PVI [67, 68, 69] in patients at risk of CIN due to the initially perceived non-nephrotoxicity of Gd-CM. More than 50 papers were published up to 2008. However, the non-nephrotoxicity of Gd-CM has been proved wrong [70, 71, 72] and, in fact, Gd-CM may have a higher general and renal toxicity than I-CM when used in iso-attenuating concentrations and volumes [73, 74, 75].

Though those reporting on Gd-CM for CTA, PCA, and PVI admit that its attenuation is inferior to that of routinely used I-CM concentrations, the general conclusion still is that the examinations were diagnostically acceptable and safe with regard to nephrotoxicity [67, 76]. Thus, it should be diagnostically feasible to use I-CM in concentrations and doses resulting in the same attenuation as Gd-CM, which may imply even less nephrotoxic potentials than the “non-nephrotoxic” Gd-CM and no risk of NSF.

CT angiography

The results from a phantom experiment [76] shown in Tab. 4 indicates that at 80–140 kVp CTA a concentration of about 90–125 mg I/ml would result in the same CM enhancement as a common Gd-CM concentration of 0.5 mmol/ml. An I-CM dose of 75–100 mg I/kg at 80–140 kVp would correspond to 0.4 mmol/kg Gd-CM, a relatively large Gd-CM dose proven diagnostic in various CTA reports.

Remy-Jardin et al. [66] used 80 kVp 16-MDCT with 0.4 mmol Gd/kg to perform pulmonary CTA in patients with contraindications to I-CM. This would roughly correspond to only 6.0 g-I in a 75 kg person (=75 kg × 80 mg I/kg) or 40 ml 150 mg I/ml. Esteban et al. [65] used 120 kVp 16-MDCT with a mean dose of about 0.4 mmol Gd/kg for aortic CTA corresponding to 50 ml 140 mg I/ml (7 g-I) in a 75 kg person.

Percutaneous catheter angiography and interventions

Angiographic phantom experiments at 60, 70, 80, 95, and 115 kVp indicate that iodine concentrations of 35, 60, 70, 80 and 90 mg/ml, respectively, are iso-attenuating with 0.5 M Gd-CM (Fig. 2, [76]). Note that if the x-ray tube potential is lowered to 60 kVp, only 35 mg I/ml may be required to examine the femoral, popliteal, and lower leg arteries (see Fig. 7 in reference [67]). According to literature reports aortic, peripheral, renal, and carotid PCA/PVI have been successfully performed with mean doses of 0.2–0.8 mmol Gd/kg or about 30–124 ml 0.5 M Gd-CM, corresponding to 30–124 ml 70 mg I/ml (2.1–8.7 g-I) at 80 kVp [76].

Coronary angiography has been performed with 1.0 M Gd-CM [69] corresponding to 140 and 180 mg I/kg at 80
and 115 kVp, respectively. Thus, coronary procedures may be performed with half the routinely used concentrations (~320–370 mg I/ml), especially in thinner patients in whom automatic dose regulation of x-ray tube potential increases iodine attenuation.

**Meticulous technique to save contrast media**

Experiences obtained at 80 kVp pulmonary CTA and from using Gd-CM in CTA and PCA/PVI indicate that diagnostic studies in azotemic patients should be able to obtain using I-CM in substantially lower concentrations and doses than in common practice. This requires meticulous examination technique and may include the adjunct of carbon dioxide as CM in PCA/PVI [77, 78].

**Infoboxes 1 and 2** summarize some precautions and techniques to accomplish this in CTA and PCA/PVI.

**Conclusions**

- Renal function should be estimated taking into account not only serum creatinine but also age, gender, ethnicity, and body size by using dedicated GFR prediction equations.
- CM dose should be expressed in grams of iodine (g-I) taking into account concentration apart from volume and serves as an index of diagnostic capacity.
- In general a g-I/eGFR ratio ≥ 1.0 appears to a significant and independent predictor of CIN in coronary interventions but it may also be valid for peripheral (non-renal) PCA/PVI and CTA.
- Extra caution is warranted for selective renal, and juxta-/supraparenal aortic injections since high-concentrated CM may affect the kidneys and plasma isotonic CM should be used to avoid hypertonic nephrotoxic effects.
- If a CM examination is deemed necessary in patients at high risk of CIN, it is the author’s goal to keep the dose as low as reasonably achievable below a g-I/eGFR ratio of 0.5, which may be possible by applying a meticulous ex-

**Corresponding address**

U. Nyman
Department of Diagnostic Radiology, Lasaretet Trelleborg, University of Lund 23185 Trelleborg Sweden ulf.nyman@skane.se

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