ANGIOGRAPHICALLY INDUCED RENAL FAILURE
AND ITS RADIOGRAPHIC DETECTION

Robert A. Older,1 Joseph P. Miller, Donald C. Jackson, Irwin S. Johnsrude,
and William M. Thompson

ABSTRACT:
Decreased renal function following arteriography is much more common than is
currently realized. Steps to detect this failure are necessary, especially in high risk
patients, so that stressful situations such as surgery can be avoided. A recently per-
formed prospective random study of 100 patients undergoing angiography demon-
strated a 10% incidence of renal failure. Those patients most at risk had preexisting
renal disease as indicated by an elevated serum creatinine and/or cardiovascular
disease severe enough to require digoxin, diuretics, or nitroglycerin. No cases of
renal failure occurred in the absence of one or both of these processes. The likelihood
of postangiographic renal failure was unrelated to the quantity of contrast as
measured either by total volume or per kilogram body weight.

INTRODUCTION
Toxicity of intravenous contrast media has been a matter of concern since the tech-
nique was first used. In the 1950s and early 1960s the serious and frequent complica-
tion of renal failure secondary to admin-
istration of angiographic contrast media was recognized and documented by pro-
spective studies [1–6]. With the introduc-
tion of newer and safer contrast media, the incidence of renal failure diminished and
was no longer considered a major problem
[7–12]. Although renal toxicity has been demonstrated with the newer media both
clinically and experimentally [13–15], studies indicate that current contrast is safe (table
1). Recently Port et al. [20] reported eight
cases of renal failure secondary to arteriog-
raphy. This was not a high incidence con-
sidering that 7,400 studies were performed
over a period of 6 years. This was a retro-
spective study, however, and the authors
suggested that there may have been a consi-
derably higher incidence than detected.
Two recent cases of renal failure were de-
tected in rapid succession in our hospital.
Both occurred immediately postangiog-
raphy, and both were initially uncovered in
our radiology department on the basis of a
persistent 24-hr nephrogram. Stimulated
by these observations, a prospective study
on 100 randomly chosen patients was un-
dertaken to determine the incidence of
renal failure after angiography. This paper
reports the results of this study.

MATERIALS AND METHODS
A 24-hr postangiogram abdominal film was
used as the initial method of detection of renal
failure. A persistent nephrogram indicates poor
excretion of the contrast and has been shown
to be associated with renal failure [22] (fig. 1).
The film of the abdomen was obtained on 100
random patients undergoing various types of
arteriography. The contrast media used were
salts of diatrizoates or iothalamates in concen-
trations and amounts within generally ac-
cepted levels. A 24-hr film was reviewed by
one of us. When a persistent nephrogram was
observed, serum creatinines were obtained for
three consecutive days. Creatinines were not
routinely obtained in patients without a posi-
tive nephrogram. A preangiographic creatinine
level greater than 1.2 mg/100 ml was used as
the criterion for preexisting renal disease. De-
terioration in renal function subsequent to an
angiogram was considered to have occurred if

1 Presented at the annual meeting of the American Roentgen Ray Society, Atlanta, Georgia, October 1975.
W. M. Thompson is a James Picker Foundation Scholar.
1 All authors: Department of Radiology, Duke University Medical Center, Durham, North Carolina 27710.
Older et al.

Table 1: Renal Failure Due to Contrast Media

<table>
<thead>
<tr>
<th>Reference</th>
<th>Year</th>
<th>Contrast</th>
<th>Type of Study</th>
<th>No. Studied</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Miller et al. [6]</td>
<td>1953</td>
<td>Diiodinated</td>
<td>Translumbar</td>
<td>250</td>
<td>4</td>
<td>1.6</td>
</tr>
<tr>
<td>Edling and Helander [2]</td>
<td>1957</td>
<td>Triiodinated</td>
<td>Abdomen-renal</td>
<td>13,207</td>
<td>39</td>
<td>0.3</td>
</tr>
<tr>
<td>Bartley et al. [16]</td>
<td>1969</td>
<td>Triiodinated</td>
<td>Abdomen</td>
<td>302</td>
<td>7</td>
<td>2.1</td>
</tr>
<tr>
<td>Reiss et al. [18]</td>
<td>1972</td>
<td>Triiodinated</td>
<td>Abdominal-renal</td>
<td>2,710</td>
<td>8</td>
<td>0.29</td>
</tr>
<tr>
<td>Port et al. [20]</td>
<td>1974</td>
<td>Triiodinated</td>
<td>Abdominal-peripheral</td>
<td>7,400</td>
<td>8</td>
<td>0.1</td>
</tr>
<tr>
<td>Brewster et al. [21]</td>
<td>1975</td>
<td>Triiodinated</td>
<td>Abdomen</td>
<td>190</td>
<td>1</td>
<td>0.5</td>
</tr>
</tbody>
</table>

* Prospective study.

The serum creatinine level changed by at least 20% or 0.3 mg/100 ml.

Results

Of the 100 patients initially in the study, 10 were eliminated because of insufficient data. Of the remaining 90, 17 had a positive nephrogram at 24 hr. Nine of the 17 showed a significant change in renal function, indicating a 10% incidence of renal failure. Table 2 and figures 2 and 3 show the change in serum creatinine levels in these nine patients. One patient was oliguric for 24 hr but due to laboratory error, renal function studies were not obtained until the failure had been resolved. The incidence of failure detected was considerably higher than has been reported with current contrast media [16–21].

Additional Data

During the 4 months of the prospective study, five patients not included in our random selection also developed clinically documented renal failure following angiography (table 2 and fig. 4). Of this combined group of 14 patients, 10 had renal failure of sufficient magnitude to be life threatening, especially if they were to be subjected to further stress.

The amount of contrast media used and the type of angiographic study performed in this combined group of patients are summarized in table 3. Possible predisposing factors are listed in table 4.

Case Reports

Case 1

B. D. (patient no. 14) had an aortofemoral arteriogram for evaluation of peripheral vascular disease. The patient was being treated with digoxin for congestive heart failure. Renal function was within normal limits with a serum creatinine level of 1 mg/100 ml prior to the angiogram. During angiography, the patient received 100 cm³ of Renografin 60 and 100 cm³ of Renografin 76 (2.0 cm³/kg body weight). The morning following angiography, the patient's serum creatinine level was 3.0 mg/100 ml, but this result was not available prior to surgery. Immediately following surgery the

Fig. 1.—Persistent nephrogram 24 hr after arteriography. Contrast in gallbladder is from catheterization; patient did not have gallbladder study.
TABLE 2

Changes in Renal Function after Angiography

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Increase in Serum Creatinine</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mg/100 ml</td>
</tr>
<tr>
<td>Primary study:</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>2.1</td>
</tr>
<tr>
<td>2</td>
<td>2.5</td>
</tr>
<tr>
<td>3</td>
<td>0.5</td>
</tr>
<tr>
<td>4</td>
<td>1.0</td>
</tr>
<tr>
<td>5</td>
<td>0.6</td>
</tr>
<tr>
<td>6</td>
<td>0.5</td>
</tr>
<tr>
<td>7</td>
<td>0.3</td>
</tr>
<tr>
<td>8</td>
<td>2.1</td>
</tr>
<tr>
<td>9*</td>
<td></td>
</tr>
<tr>
<td>Additional cases:</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>1.4</td>
</tr>
<tr>
<td>11</td>
<td>3.3</td>
</tr>
<tr>
<td>12</td>
<td>5.8</td>
</tr>
<tr>
<td>13</td>
<td>3.0</td>
</tr>
<tr>
<td>14</td>
<td>2.0</td>
</tr>
</tbody>
</table>

* Oliguric but insufficient laboratory data.

A patient developed severe renal failure (creatinine = 6.5 mg/100 ml) which returned to normal on the ninth postoperative day.

Comment. It is important to detect changes in renal failure following arteriography so that stressful situations which may lead to further renal failure and even death may be avoided. Surgery is the most common form of such stress. It is not at all unusual to have angiography performed the day prior to surgery without reevaluation of the patient's renal status between the two events. The complication of significant renal failure may have been avoided if the laboratory results had been known prior to the operation.

Case 2

E. B. (patient no. 8) was evaluated angiographically for brachiocephalic, renal vascular, and aortofemoral occlusive disease. She had mild renal insufficiency (serum creatinine of 1.5 mg/100 ml) at the time of the study. She received 340 cm$^3$ of Renografin 76 and 40 cm$^3$ of Renografin 60 (4.3 cm$^3$/kg body weight). Following arteriography, renal failure was detected on the basis of the 24-hr abdominal film. Renal function studies showed a 140% elevation of serum creatinine to 3.6 mg/100 ml. These renal abnormalities cleared with diuretics and fluids in approximately 4–5 days. Since the surgery was not an emergency, she was discharged and returned 6 weeks later for an
Multiple 178 4
Multiple I 3.8
3
2
410
Multiple 225 6
I
OLDER 3
3
4.3
Multiple
The
270 2.7
5.0
TYPE I
190

of Horsfall erable occurring promptly rising was elective procedure. Her creatinine at this time was still elevated (2.2 mg/100 ml). Following aortofemoral bypass surgery, she developed further renal deterioration with the creatinine rising to 2.9 mg/100 ml. However, this returned promptly to her previous level.

Comment. In this patient, knowledge of the renal failure prior to surgery allowed the elective operation to be delayed and may have prevented more severe renal damage from occurring after surgery.

DISCUSSION

The pathogenesis of renal failure following contrast injection has received considerable attention. Several mechanisms have been postulated: precipitation of Tamm-Horsfall proteins [22, 23]; increased blood viscosity due to aggregation and clumping of red cells [24–27]; direct toxic effect on the renal tubules [7, 28, 29]; allergic reactions including antibodies to sodium iothalamate [30, 31]; uricosuric effect [32]; and anoxia due either to replacement of oxygenated blood by contrast or to a shift of the oxyhemoglobin curve to the left [33].

Osmotic nephrosis has been detected after contrast studies, but the relationship of this histologic entity to clinical renal failure is not certain [34]. The importance of each of the above in renal failure due to contrast media is uncertain.

Prior to angiography, those patients who are most likely to develop renal compromise as the result of the procedure should be identified. Our study indicates that the patient most at risk is hypertensive, has preexisting renal disease as evidenced by elevated serum creatinine, has some form of cardiovascular disease severe enough to require digoxin, diuretics, or nitroglycerin, and may be in congestive heart failure (table 4). In our series, no patient had multiple myeloma, and only one had hyperuricemia. The role of diabetes mellitus may be significant, since four of the 14 patients had this disease.

Ten of the 14 patients who developed renal failure had preexisting renal disease (table 4). This has prompted us to obtain serum creatinines prior to all angiographic procedures. The clinical review of systems was most often negative with regard to preexisting renal disease and is not by itself a

<table>
<thead>
<tr>
<th>TABLE 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANGIOGRAPHIC DETAILS IN PATIENTS WITH RENAL FAILURE</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Amount of Contrast</th>
<th>Type of Angiographic Study*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient No.</td>
<td>Body Weight (cm²/kg)</td>
</tr>
<tr>
<td>1</td>
<td>2.0</td>
</tr>
<tr>
<td>2</td>
<td>3.6</td>
</tr>
<tr>
<td>3</td>
<td>1.9</td>
</tr>
<tr>
<td>4</td>
<td>2.7</td>
</tr>
<tr>
<td>5</td>
<td>4.6</td>
</tr>
<tr>
<td>6</td>
<td>3.1</td>
</tr>
<tr>
<td>7</td>
<td>1.9</td>
</tr>
<tr>
<td>8</td>
<td>4.3</td>
</tr>
<tr>
<td>9</td>
<td>3.8</td>
</tr>
<tr>
<td>10</td>
<td>4.1</td>
</tr>
<tr>
<td>11</td>
<td>2.7</td>
</tr>
<tr>
<td>12</td>
<td>5.0</td>
</tr>
<tr>
<td>13</td>
<td>1.4</td>
</tr>
<tr>
<td>14</td>
<td>2.8</td>
</tr>
</tbody>
</table>

*Multiple = flush aortogram and at least one selective injection.
sufficient technique for screening.

Cardiovascular disease was present in 12 of the 14 patients who developed renal failure (table 4). Of these 12 patients, nine had arteriosclerotic vascular disease manifested by transient cerebral ischemic attacks, angina, or claudication. One patient had severe rheumatic heart disease with two prosthetic valves, one had severe renal vascular hypertension, and one had nephrotic syndrome complicated by congestive heart failure. While only five of these 12 patients had congestive heart failure, all 12 had cardiovascular disease significant enough to require digoxin, diuretics, or nitroglycerin.

The generally accepted upper limits of dose tolerance for contrast media in an angiographic study vary up to a total of 5 cm³/kg body weight during the entire procedure. In our series (table 3), renal failure developed in patients who received as little as 1.4 cm³/kg (85 cm³ total) during a cardiac catheterization. Although as much as 5 cm³/kg was given in one patient, the average dose in patients entering into renal failure was 3 cm³/kg.) No correlation was seen between the amount of contrast (either total or per kilogram body weight) and the severity or likelihood of developing renal failure.

No single angiographic procedure predisposed the patient to postangiographic renal failure. Two of the patients had aortofemoral arteriograms, one had cardiac catheterization, three had arch arteriograms, and nine had multiple injections, including at least one selective renal injection in six. One of the 14 patients had an obvious allergic reaction to the contrast media, developing a mild urticaria which responded promptly to parenteral Benadryl. In no case was sustained hypotension documented during any of the angiographic procedures.

Patients are often fasted after midnight while in the hospital. Specific clear liquid breakfast orders are routine prior to angiography in our department. No doubt many patients were inadvertently fasted for variable periods prior to angiography, and we are unable to comment upon the significance of dehydration in contributing to renal failure.

Several patients had other contrast studies (intravenous pyelography, cardiac catheterization, etc.) the day before or after angiography. In light of our findings, this

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Primary Diagnosis</th>
<th>Preexisting Renal Disease</th>
<th>Congestive Heart Failure</th>
<th>High Blood Pressure</th>
<th>Cardiovascular Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Nephrotic syndrome</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Digoxin, diuretics</td>
</tr>
<tr>
<td>2</td>
<td>ASCVD</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Lanoxin, diuretics</td>
</tr>
<tr>
<td>3</td>
<td>Renovascular hypertension</td>
<td>+</td>
<td>...</td>
<td>+</td>
<td>Antihypertensives, Inderal</td>
</tr>
<tr>
<td>4</td>
<td>Hypernephroma</td>
<td>+</td>
<td>...</td>
<td>...</td>
<td>None</td>
</tr>
<tr>
<td>5</td>
<td>ASCVD, mitral regurgitation</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>Digoxin, Persantine</td>
</tr>
<tr>
<td>6</td>
<td>Aortic aneurysm</td>
<td>...</td>
<td>...</td>
<td>+</td>
<td>Digoxin, diuretics</td>
</tr>
<tr>
<td>7</td>
<td>ASCVD, rheumatic heart disease</td>
<td>...</td>
<td>+</td>
<td>+</td>
<td>Inderal, nitroglycerine</td>
</tr>
<tr>
<td>8</td>
<td>ASCVD</td>
<td>...</td>
<td>...</td>
<td>+</td>
<td>Diuretics, antihypertensives</td>
</tr>
<tr>
<td>9</td>
<td>ASCVD</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>Digoxin, nitroglycerine</td>
</tr>
<tr>
<td>10</td>
<td>left hydronephrosis, CAD</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Nitroglycerine</td>
</tr>
<tr>
<td>11</td>
<td>ASCVD</td>
<td>+</td>
<td>...</td>
<td>+</td>
<td>Digoxin, diuretics</td>
</tr>
<tr>
<td>12</td>
<td>Bilateral hydronephrosis</td>
<td>+</td>
<td>...</td>
<td>+</td>
<td>None</td>
</tr>
<tr>
<td>13</td>
<td>Endocarditis, mitral and aortic regurgitation</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Digoxin, diuretics</td>
</tr>
<tr>
<td>14</td>
<td>ASCVD</td>
<td>...</td>
<td>+</td>
<td>+</td>
<td>Digoxin</td>
</tr>
</tbody>
</table>
added insult to the kidneys could only be detrimental and may under some circumstances have been the deciding factor as to whether the patient developed renal failure. Several days should elapse between contrast studies if the patient’s condition permits. When delay is not possible, the patient should be carefully monitored for renal failure for several days.

The importance of the positive nephrogram should be considered: 53% of our patients who showed contrast media lying within the renal parenchyma on the 24-hr films had documented renal failure. Chart review of the majority of cases without a positive nephrogram, and in whom routine laboratory studies were not obtained, revealed no instances of clinical renal failure. Sufficient laboratory data was available for 30% of these patients to exclude subclinical renal failure.

We are currently performing a larger study which includes a renal profile both before and after arteriography in all patients studied rather than just those with a positive nephrogram. This will give a broader appreciation of the full scope of the problem of renal failure as it relates to angiography. The profile includes a KUB using identical geometry and radiographic factors before and after angiography. This should provide a better baseline for more accurate determination of a positive nephrogram. The role of the KUB as a sensitive tool in the investigation of postangiographic renal failure will thus be more accurately evaluated.

REFERENCES

2. Edling NPG, Helander CG: On renal damage due to angiography and its detection by renal tests: with reports of five cases of severe renal damage. Acta Radiol 47:473-480, 1957
22. Berdon WE, Schwartz RH, Becker J, Baker DH: Tamm-Horsfall proteinuria; its relation-


This article has been cited by:


4. Richard W. Katzberg, Wayne L. Monsky, Nicolas D. Prionas, Vishal Sidhar, Jeffrey Southard, Janine Carlson, John M. Boone, Tzu-Chun Lin, Chin-Shang Li. 2012. Persistent CT nephrograms following cardiac catheterisation and intervention: initial observations. *Insights into Imaging* 3:1, 49-60. [Crossref]


7. Peter McCullough, Sandeep Soman. Epidemiology and predictors of contrast-induced nephropathy 19-33. [Crossref]


9. Barbara Elmståhl, Ulf Nyman, Peter Leander, Chun-Ming Chai, Bo Frennby, Torsten Almén. 2004. Gadolinium contrast media are more nephrotoxic than a low osmolar iodine medium employing doses with equal x-ray attenuation in renal arteriography: An experimental study in pigs. *Academic Radiology* 11:11, 1219-1228. [Crossref]


11. Mohammed A. Quader, Carol J. Sawmiller, Bauer A. Sumpio. Radio Contrast Agents: History and Evolution 775-783. [Crossref]


17. D. Maruhn, S. Hahnemann. Nephrotoxizität: Die Rolle der klinisch-chemischen Diagnostik 104-114. [Crossref]


20. GEORGE W. VETROVEC, DOUGLAS M. LANDWEHR, VIRGINIA L. EDWARDS. 1989. Incidence of Renal Artery Stenosis in Hypertensive Patients Undergoing Coronary Angiography. *Journal of Interventional Cardiology* 2:2, 69-76. [Crossref]

22. C. J. Powell, M. Dobrota, E. Holtz. Studies on the Mechanism of Radiological Contrast Media Induced Renal Failure 463-468. [Crossref]
26. Vito M. Campese, Kunitoshe Iseki. Contrast-Induced Acute Renal Failure 135-144. [Crossref]
27. K. Golman, E. Holtz, T. Almén. Radiographic Contrast Media 701-725. [Crossref]
30. Mark H. Gardenswartz, Jan P. Goldberg, Robert W. Schrier. Drug-Induced Nephrotoxicity 365-380. [Crossref]
33. K. Golman, T. Almén. Urographic Contrast Media and Methods of Investigative Uroradiology 127-191. [Crossref]
34. Michael A. Bettmann. Complications of Angiography in the Thorax 175-186. [Crossref]
35. L. Diethelm, H. Fritz. Toxische Osteopathien 649-815. [Crossref]
36. L. Diethelm, H. Fritz. Toxische Osteopathien 649-815. [Crossref]
38. Daniel A. Feeney, Don L. Barber, Carl A. Osborne. 1982. THE FUNCTIONAL ASPECTS OF THE NEPHROGRAM IN EXCRETORY UROGRAPHY: A REVIEW. Veterinary Radiology 23:2, 42-45. [Crossref]
41. David W. Gelfand, David J. Ott, Thomas H. Hunt. Gastrointestinal Complications of Radiologic Procedures 91-122. [Crossref]
48. Donald L. Roback. 1978. CAUTION WITH CONTRAST MEDIA: The Lancet 311:8074, 1153. [Crossref]
52. Lars Tejler, Mats Ekberg, Torsten Almén, Stig Holtås. 1977. Proteinuria Following Renal Arteriography. *Acta Medica Scandinavica* 202:1–6, 131-133. [Crossref]