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Image quality and contrast agent exposure in cardiac computed tomography angiography prior to transcatheter aortic valve implantation procedures using different acquisition protocols

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ABSTRACT

Background: ECG-gated cardiac computed tomography angiography (CCTA) has found widespread use for prosthesis sizing before transcatheter aortic valve implantation (TAVI). However, still little data exists on the optimal scan-strategy in such patients. We hypothesized that prospectively triggered CCTA can enable the visualization of aortic valve structures and peripheral arteries with lower radiation and contrast agent exposure in patients considered for TAVI compared to retrospectively gated protocols.
Methods: All studies were performed using a 256 multi-detector single source CT (iCT Philips, Best, Netherlands). With the prospective protocol the whole volume from the heart to the iliofemoral arteries scanned using prospective triggering. With the retrospective protocol a first retrospectively gated scan was performed for the heart and the iliofemoral part was subsequently scanned using a second non-triggered scan. Image quality was assessed semi-quantitatively and signal-to-noise- (SNR) and contrast-to-noise-ratios (CNR) were obtained for all scans.
Results: Prospective CCTA was performed in 74 and in 34 patients, respectively using non-tailored and BMI adapted scans, whereas retrospective CCTA was performed in 57 patients. Prospective scans required lower contrast agent administration compared to retrospective scans (71 ± 8 mL versus 91 ± 15 mL, $p < 0.01$) and resulted in lower radiation exposure (26 ± 7mSv for retrospective versus 15 ± 3mSv for non-tailored prospective versus 8 ± 4mSv for BMI-adapted prospective scans, $p < 0.01$). Visual image quality was better for the evaluation of aortic valve structures and similar for the assessment of iliofemoral anatomy with prospective versus retrospective scans. In addition, contrast density, SNR and CNR were higher in the ascending aorta with prospective versus retrospective CCTA (434 ± 98HU versus 349 ± 112HU; 35 ± 14 versus 24 ± 9 and 31 ± 11 versus 16 ± 7, $p < 0.001$ for all). Subsection analysis by heart rate groups demonstrated that both image quality and CNR were significantly higher in patients with prospective versus retrospective CCTA, irrespective of the heart rate during image acquisition.
Conclusion: Prospectively triggered CCTA allows for improved visualization of aortic valve structures and peripheral arteries in patients scheduled for TAVI with simultaneously reduced contrast agent dose and radiation exposure. Therefore, this acquisition mode seems to be the preferred for the evaluation of patients considered for TAVI.

1. Introduction

Transcatheter aortic valve implantation (TAVI) has evolved as an important alternative treatment option for high and possibly moderate risk patients with severe aortic stenosis. [1–3] In contrast to surgery however, where sizing is performed under direct visualization of the aortic root, pre-procedural imaging using either echocardiography or computed tomography angiography is essential prior to TAVI to minimize periprocedural complications. [4–6] Thus, prosthesis sizing can prevent complications such as occlusion of the coronary ostia, annular

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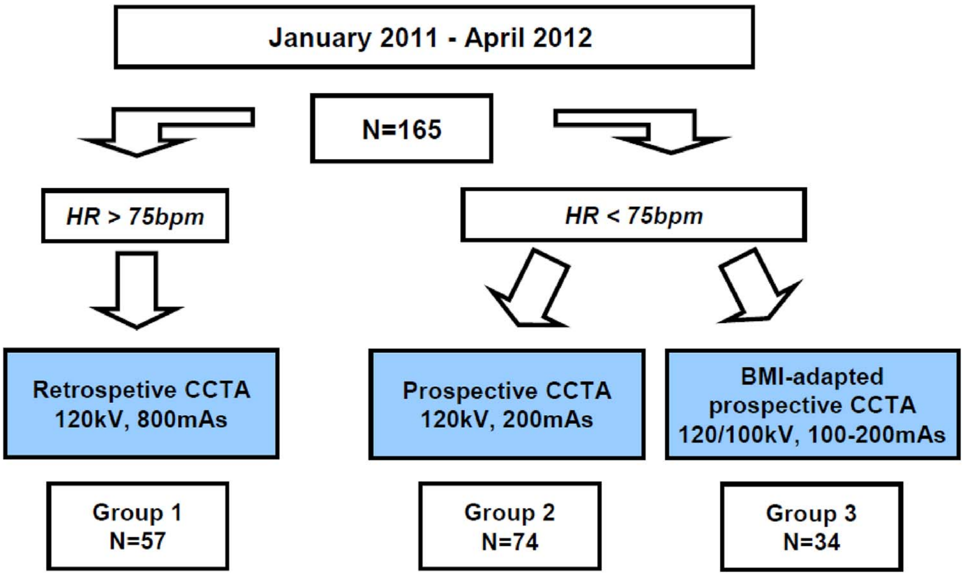

Fig. 1. Flow-chart including 57 patients who underwent retrospective, 74 patients who underwent non-tailored prospective and 34 patients who underwent BMI-adapted prospective CCTA acquisitions and were systematically analyzed in terms of radiation exposure and image quality.

rupture, device dislodgement and paravalvular regurgitation. [7,8]

The aortic annulus is anatomically defined as a virtual ring with 3 anatomical anchors at the nadir of each aortic leaflet. Its complex 3D-geometry and its crown-like and simultaneously elliptical shape may therefore limit the accuracy of 2D-measures by transthoracic or trans-esophageal echocardiography. [9] Technical developments with cardiac computed tomography angiography (CCTA) on the other hand, have recently enabled the accurate assessment of aortic valve structures in patients considered for TAVI. [6] However, contrast agent dose and radiation exposure raise concerns for the use of CCTA in patients considered for TAVI, especially in those with reduced renal function, which is quite common in such patients.

In the present study, we therefore sought to investigate the influence of different CCTA scanning protocols in terms of contrast agent and radiation exposure and on the resultant image quality for the assessment of aortic valve structures. We compared subjective image quality, signal-to-noise (SNR), contrast-to-noise ratios (CNR), and contrast agent and radiation exposure with 256-slice CCTA using retrospectively gated versus prospectively triggered protocols.

2. Methods

2.1. Study population

The study group included 165 consecutive patients with symptomatic severe aortic stenosis between January 2011 and September 2012 who underwent CCTA prior to TAVI. They were systematically analyzed in terms of contrast agent, radiation exposure and resultant image quality. Patient body weight and height were recorded at the time of the CCTA. All procedures complied with the Declaration of Helsinki, were approved by our local ethic committee and all patients gave written informed consent.

2.2. 256-slice CT scans

CCTA scans were performed using a 256-slice Brilliance iCT scanner (Philips Healthcare) that features a gantry rotation time of 270 ms, resulting in a temporal resolution of 36–135 ms, depending on the heart rate of the patient and the performance of multi-segment reconstruction algorithms, and an isotropic sub-millimeter spatial resolution.

For CCTA a bolus of the contrast agent (Ultravist 370, Bayer Schering Pharma) was injected intravenously using an antecubital I.V. line. The contrast agent was injected at a flow of 4 mL/sec followed by a saline flush (50 mL at a flow of 5 mL/s). The scan started automatically using a bolus tracking with a region of interest placed in the descending aorta and a threshold of 110 Hounsfield Units (HU). The entire volume of the heart was acquired during one breath-hold in 4–7 s with simultaneous ECG recording. The detector collimation was $2 \times 128 \times 0.625$ mm, with 256 overlapping slices of 0.625 mm thickness and dynamic z-focal spot. No premedication with ß-blockers or nitrates was given due to severe aortic stenosis in all patients.

Study design acquisition. A flow chart illustrating the 3 different acquisition protocols used in our study is provided in Fig. 1.

Patients with a heart rate ≥ 75bpm before CCTA (Group 1, n = 57), underwent a retrospectively EGC-gated helical scan of the heart (tube voltage 120 kV, tube current of 800mAs), which was then followed, after a time delay of 8–10 s, by an untriggered scan of the lower abdominal aorta and the peripheral iliofemoral vessels (tube voltage 120 kV, tube current of 200mAs).

Patients with heart rate < 75bpm before CCTA were randomly assigned to non-tailored prospectively triggered CCTA (Group 2, n = 74) (tube voltage 120 kV, tube current of 800mAs) versus BMI-adapted prospectively triggered CCTA (Group 3, n = 34) (tube voltage 100 kV, tube current of 100–200mAs, depending on patient habitus and using the iDose technique for image reconstruction. [10] In both Group 2 and 3 a single prospectively triggered CCTA scan was used for full coverage from the heart down to the peripheral iliofemoral vessels.

With prospective scans, diastolic images (75% of the cardiac cycle) were used for assessment of aortic valve structures. With retrospective scans both systolic (40% of the cardiac cycle) and diastolic images (75% of the cardiac cycle) were used, and the images with the higher quality for the evaluation of the aortic valve were considered. Representative images of a patient who underwent a retrospectively EGC-gated helical scan (a-d) and of a patient who underwent prospectively triggered CCTA (e-h) can be appreciated in Fig. 2.

2.3. Estimation of the radiation exposure

The dose-length product (DLP) was obtained from the patient dose report. The effective dose was calculated for all scans, based on DLP and an average organ weighting factor for the chest as the investigated anatomic region ($k = 0.014$ mSv × (mGy × cm)$^{-1}$) averaged between male and female models. [11] Hereby, it should be noted that a uniform conversion coefficient for all images is not entirely accurate as it does not account for all different conditions and factors in each individual examination.

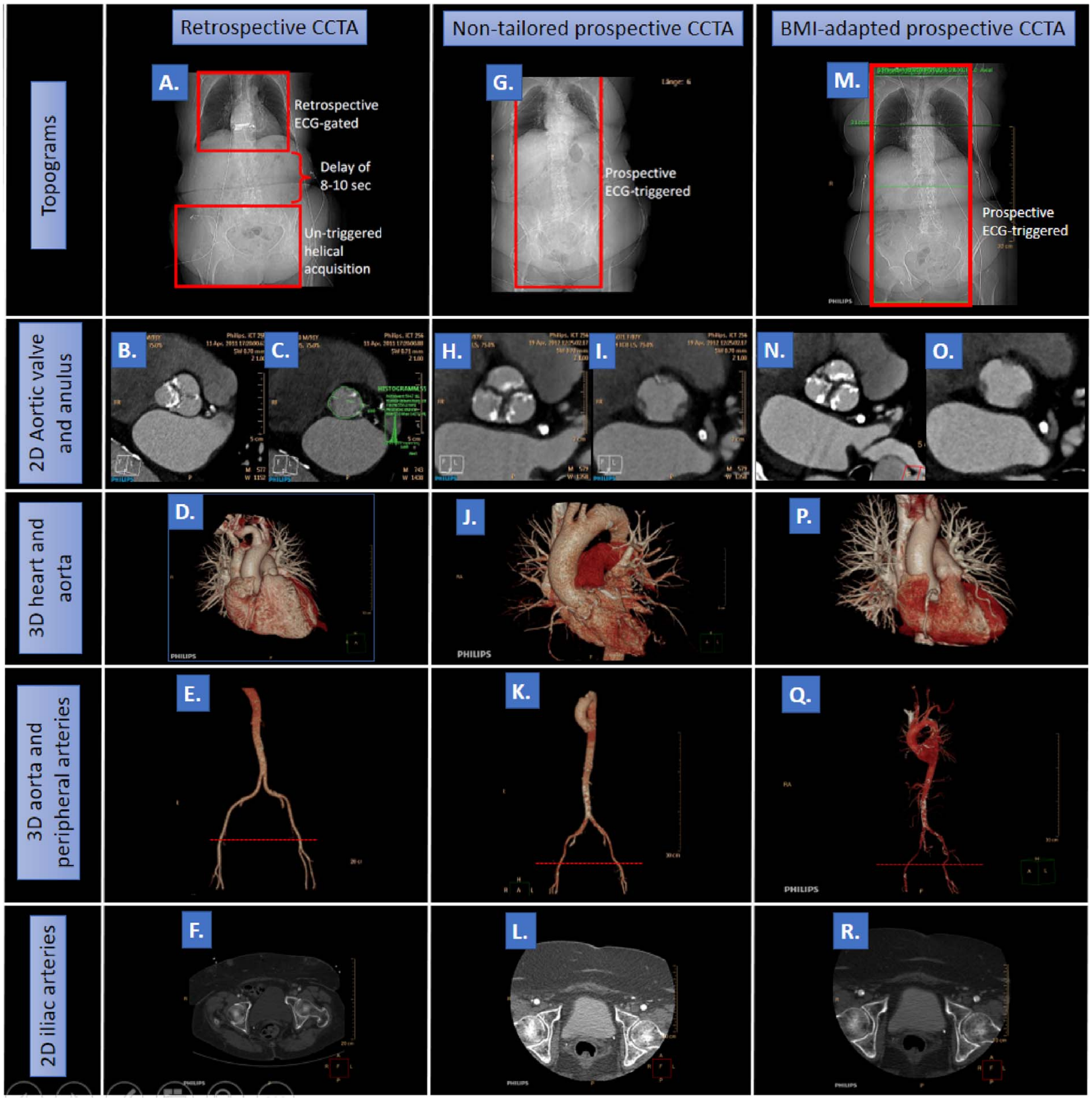

Fig. 2. Representative images of a retrospectively EGC-gated (A-F), a prospectively triggered non-tailored (G-L) and a BMI-adapted prospective CCTA protocol (M-R).

2.4. Subjective image quality

All CT data sets were analyzed using commercially available software (Philips Extended Brilliance Workspace 4.5, Cleveland, OH, US). Image quality of aortic valve structures and of the peripheral iliofemoral arteries was determined using a 5-point scale for all four groups by 2 blinded experienced readers (NHP and GK) in consensus, based on the presence of motion artefacts and image noise influencing subjective image quality:

1 = excellent image quality, i.e. no visible effects of noise or artefacts,

2 = good image quality, i.e. minimal visible effects of noise or artefacts

3 = moderate image quality, i.e. mild visible effects of noise or artefacts

4 = poor image quality, i.e. moderate visible effects of noise or artefacts, and

5 = extremely high noise resulting in non-diagnostic image quality

With the aortic valve, the blinded readers focused on evaluability of the aortic annulus, the ostia of the coronary arteries and of the ascending aorta. With peripheral arteries, the readers focused on evaluability of the peripheral access site for TAVI, including vessel diameter, potential stenosis and calcification.

Inter- and intra-observer variability for assessment of aortic valve structures, including annulus short axis, coronal and long axis diameter, eccentricity, distance between the aortic annulus and the right and left coronary ostium and aortic valve calcification in our CCTA lab has been demonstrated previously. [4]

Objective image quality. Contrast density was measured in the ascending aorta and in the abdominal aorta.

Signal-to-noise ratio (SNR) was calculated as follows:

$$SNR = \frac{MeanCTdensityofthe'regionofinterest'}{Standarddeviationinthesame'regionofinterest'}$$

Contrast-to-noise ratio (CNR) was calculated as follows:

$$CNR = \frac{MeanCTdensityofthe'regionofinterest' - MeanCTdensityofadjacenttissue}{Standarddeviationofthebackgroundregion}$$

Table 1
Baseline characteristics.

	Retrospective (n = 57)	Prospective (n = 108)	p-values
	Demographic data		
Age (years)	82 ± 5	81 ± 10	NS
Male gender	25 (44%)	51 (47%)	NS
Body weight (kg)	76 ± 17	73 ± 14	NS
Height (m)	1.66 ± 0.10	1.66 ± 0.08	NS
Body-mass-Index (kg/m[2])	27 ± 6	26 ± 4	NS
	CCTA data		
Heart rate (bpm)	82 ± 15	68 ± 11	< 0.001
Annulus diameter (long axis, mm)	28 ± 3	28 ± 3	NS
Annulus diameter (short axis, mm)	25 ± 3	24 ± 3	NS
Implantation of CoreValve	35 (61%)	71 (66%)	NS
Implantation of Edwards Valve	18 (32%)	34 (31%)	NS

For SNR and CNR calculations of the heart and of peripheral arteries, regions of interest were placed in the ascending aorta or in the infra-renal abdominal aorta, respectively. For calculation of noise the background region was set in the air outside the body.

2.5. Statistical analysis

Continuous variables are expressed as mean +/− standard deviation (SD) or +/−95%CI. Categorical variables are expressed as absolute numbers and percentages (%). Differences between prospective and retrospective groups of patients were calculated using ANOVA with Bonferroni adjustment for multiple comparisons. Linear regression analysis was used for assessing the correlation between heart rate and CNR in the ascending aorta. Interobserver variability was tested in 40 randomly selected study subjects. Differences were considered statistically significant at $p < 0.05$. For parts of the statistical analysis Groups 2 and 3 are presented as one prospective CCTA group.

3. Results

3.1. Demographic parameters

An overview of our patient cohort is shown in Table 1. Most patients were female and older than 80 yrs. Except for the heart rate during CCTA acquisitions, baseline parameters were not statistically different in patients who underwent prospectively triggered versus retrospectively gated CCTA.

3.2. Contrast agent and radiation exposure

Contrast agent dose was significantly higher with retrospective compared to the standard non-tailored and BMI-adapted prospective CCTA (91 ± 15 mL in Group 1, versus 71 ± 7 mL in Group 2 and 71 ± 10 mL in Group 3, $p < 0.01$ for Group 1 versus Groups 2 & 3) (Fig. 3a). In addition, radiation exposure was highest in the retrospective group (26 ± 7mSv, $p < 0.05$ versus Group 2 & 3), followed by the non-tailored prospective CCTA (15 ± 3mSv, $p < 0.05$ versus Group 1 & 3) and by the BMI-adapted prospective Group (8 ± 4mSv, $p < 0.05$ versus Group 1 & 2) (Fig. 3b).

3.3. Visual image quality

Using prospective CCTA, significantly higher visual image quality was achieved for the assessment of aortic valve structures (2.1 ± 1.0 versus 2.9 ± 1.3, $p < 0.001$) (Fig. 4a). Conversely, the visualization of peripheral vessels, was similarly good in patients who underwent retro- versus prospective CCTA (1.6 ± 0.8 versus 1.8 ± 0.9, p = NS) (Fig. 4b).

3.4. Quantitative analysis of contrast density, SNR & CNR

Contrast density was higher both in the ascending aorta and in the infra-renal abdominal aorta with prospective versus retrospective CCTA (349 ± 112 versus 434 ± 98HU in the ascending aorta, $p < 0.001$ and 387 ± 134 versus 459 ± 126HU in the abdominal aorta, $p = 0.001$, Fig. 5a-b).

In addition, prospective scans exhibited higher SNR and CNR in the ascending aorta (Fig. 5c-d). In the abdominal aorta, SNR was

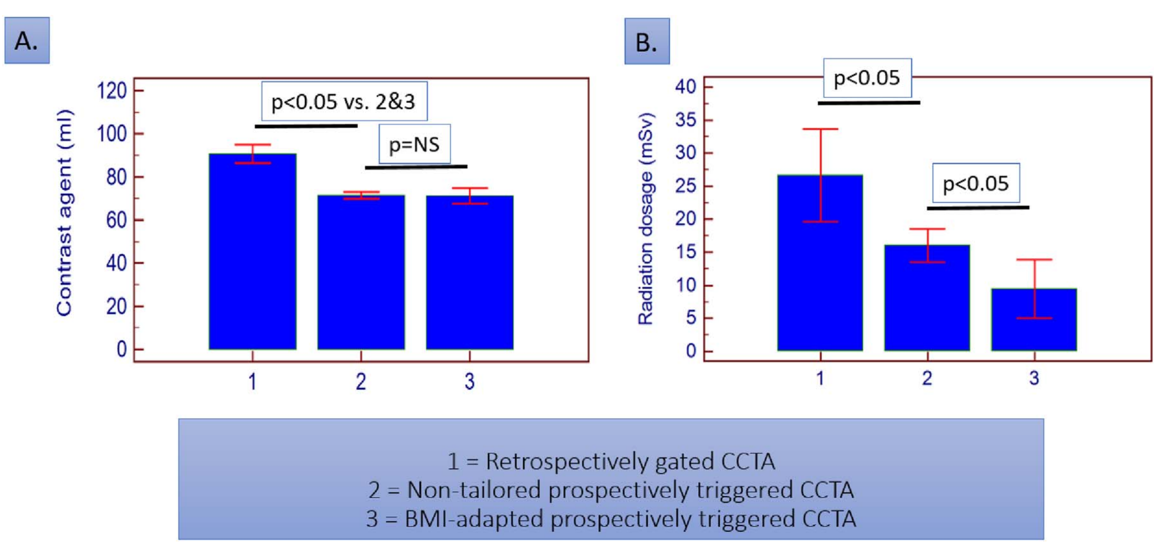

Fig. 3. Contrast agent exposure was significantly higher with retrospective compared to prospective CCTA (A). Radiation exposure was highest in the retrospective group, followed by the non-tailored prospective CCTA and was the lowest using the BMI-adapted prospective CCTA (B).

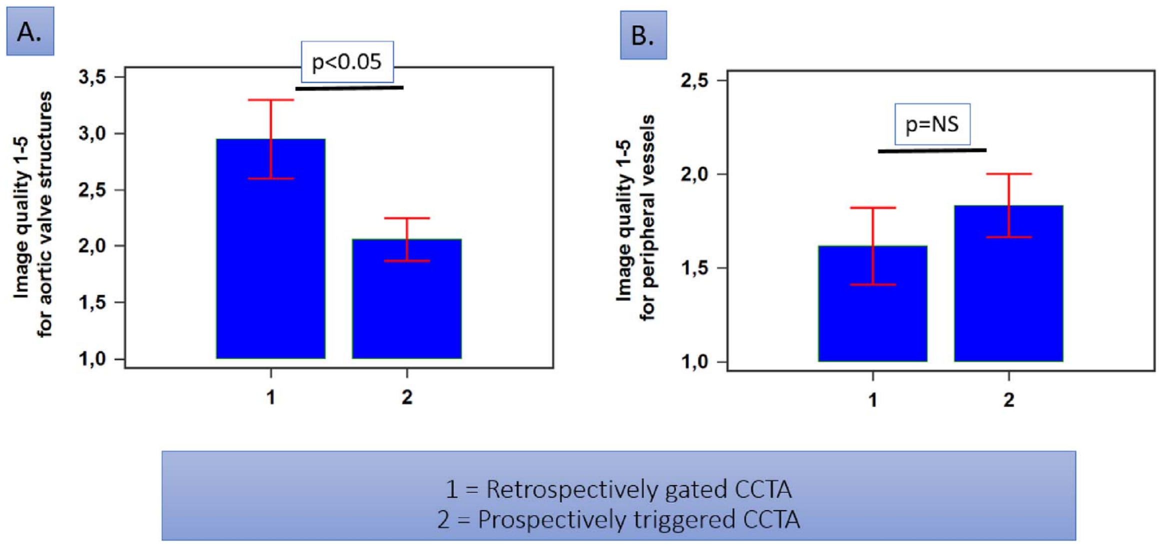

Fig. 4. Using prospective CCTA, significantly higher visual image quality was achieved for the assessment of the aortic valve (A). For the visualization of peripheral vessels, image quality was similarly good for retro- versus prospective CCTA (B).

significantly higher in the prospective groups, whereas CNR was significantly higher only in the prospective BMI-adapted group, compared to the retrospective group (Fig. 5e-f).

3.5. Subsection analysis by heart rate

Analysis by heart rate, demonstrated that CNR in the ascending aorta and image quality for the evaluation of aortic valve structures decreased with increasing heart rates ($r = -0.34$, $p < 0.001$ and $p < 0.001$ for ANOVA, respectively) (Fig. 6a-b).

Analysis by heart rate groups demonstrated that both image quality and CNR were significantly higher in patients prospective versus retrospective CCTA both in patients with heart rate < 75bpm and in those with heart rate ≥75bpm (Fig. 6c-d).

Overall, 16 (28.1%) patients who underwent retrospective CCTA exhibited heart rates < 75bmp, whereas 28 (26.0%) patients who underwent prospective CCTA exhibited heart rates ≥75bpm (Fig. 6e). Patients with heart rate < 75bmp showed similar heart rates with pro- and retrospective scans, whereas a trend for slightly higher heart rates in patients with retrospective CCTA was noted within the subgroup with heart rates ≥ 75bpm, which however did not reach statistical significance (Fig. 6f).

The exact distribution of image quality with different protocols and heart rates can be appreciated in the **supplementary** Table 1. In 11 (6.7%) cases non-diagnostic image quality was noted, which was attributed to moving artefacts with aortic valve structures (n = 8) or low contrast density in the ascending aorta (< 300HU, n = 3). Two of 108 (1.9%) patients with prospective CCTA showed non-diagnostic image quality, compared to 9 of 57 (15.8%) patients who underwent retrospective scans.

3.6. Observer variabilities

Assessment of subjective image quality yielded high inter-observer agreements of $\kappa = 0.77$. Intra- and inter-observer variability was 5%, 9% and 11% and 4%, 10% and 13%, respectively for the assessment of signal density, SNR and CNR.

4. Discussion

Cardiac computed tomography angiography (CCTA) allows for the concomitant delineation of aortic valve structures and of peripheral arteries with high spatial resolution in patients scheduled for TAVI with high spatial resolution. The main findings of our study are that:

- Retrospectively gated and prospectively triggered CTA of the heart and of peripheral iliac and femoral arteries allows the simultaneous assessment of both, aortic valve structures and vascular access site, prior to TAVI with high diagnostic image quality.
- Prospective protocols require a significantly lower amount of contrast agent volumes and are simultaneously associated with significantly lower radiation exposure for the patients compared to retrospective CCTA. The resultant image quality is similar for the assessment of the peripheral vascular access site for both protocols, whereas prospective scans even achieve higher image quality for the assessment of aortic valve structures.
- Quantitative analysis confirms visual findings, exhibiting higher values for contrast density, SNR and CNR in the ascending aorta with prospective versus retrospective CCTA.
- BMI-adapted protocols can help for further reduction in radiation exposure within prospective scans, without reducing the resultant image quality.
- Analysis by heart rate demonstrates that image quality and CNR are significantly higher in patients prospective versus retrospective CCTA both in patients with heart rate < 75bpm and in those with heart rate ≥75bpm, so that prospectively ECG-triggered protocols seem to be the first-choice acquisition mode in patients scheduled for TAVI.

4.1. Previous studies

Numerous previous studies have demonstrated the value of CCTA to offer valuable information for the evaluation of aortic root dimensions and iliac artery anatomy prior to TAVI, [4,12,13] which is crucial for procedural optimization and prevention of procedural vascular complications and postprocedural paravalvular regurgitation. Due to the high isotropic spatial resolution and fast volume coverage of modern CCTA scanners, recent studies have focused on the ability of this technique to evaluate aortic and iliofemoral anatomy with low radiation exposure and contrast agent administration. The latter is particularly important in patients considered for TAVI, because such patients frequently exhibit reduced renal function and therefore higher risk for the development of contrast induced nephropathy. [14] According to previous trials, the total amount of contrast agent for the evaluation of the aortic annulus and of iliofemoral anatomy varies between 120 and 140 mL [15–17] In some centers, either the aortic valve and the

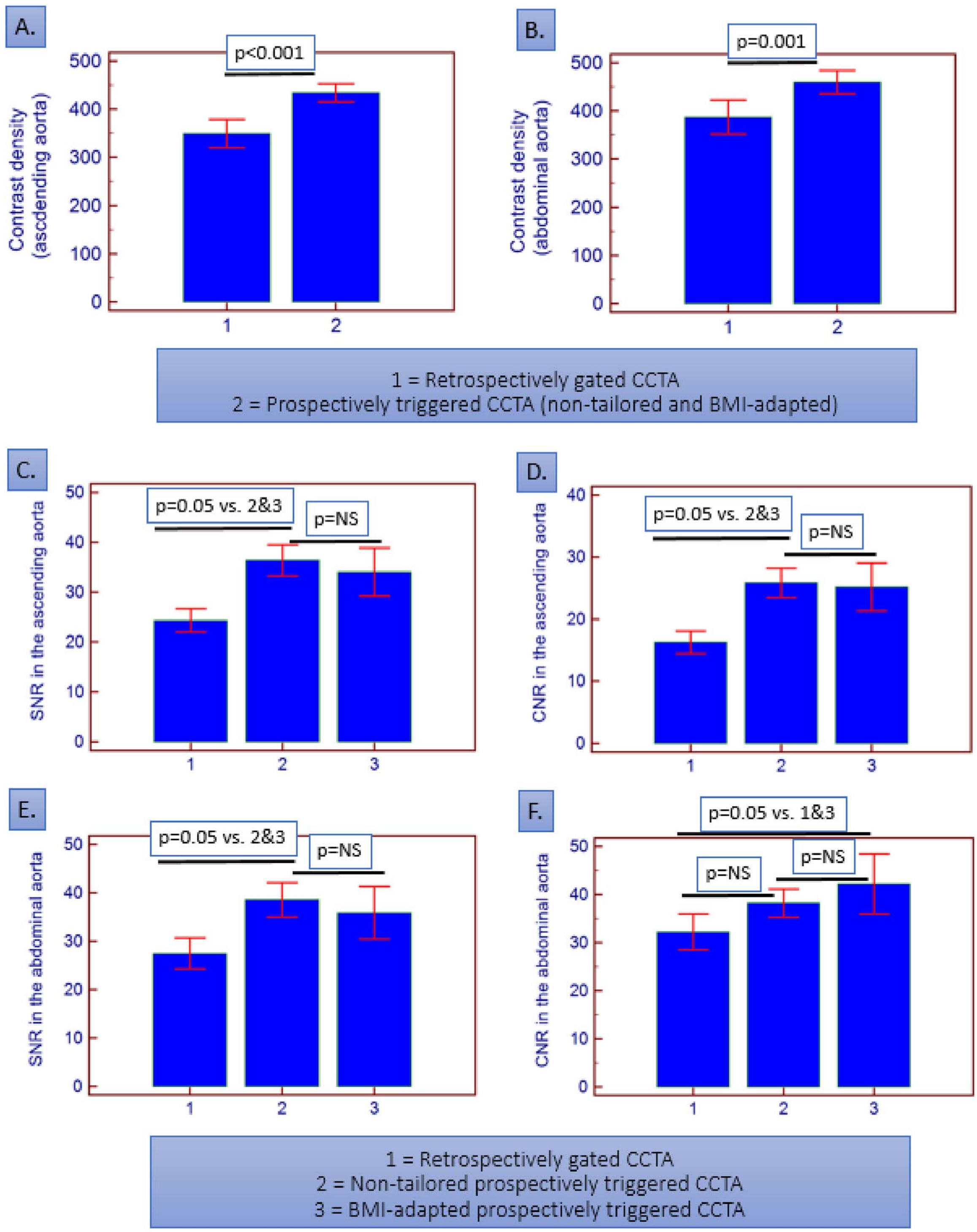

Fig. 5. Contrast density was higher both in the ascending aorta and in the lower abdominal aorta with prospective versus retrospective CCTA (A-B). Prospective scans exhibited higher SNR and CNR in the ascending aorta (C-D). In the abdominal aorta, a trend for higher values was observed favouring the prospective CCTA, which reached statistical significance for SNR but not for CNR (E-F).

peripheral arteries are scanned within a single examination, which requires high radiation exposure and more than 90 mL contrast agent. [18] Alternatively, the examination is split in two parts, including a retrospectively-gated scan of the heart, which is followed by a non-triggered helical scan of the aorta and the iliofemoral arteries. The latter approach requires less radiation but even higher contrast agent exposure over 120 mL, due to a double bolus injection required for (i) cardiac and (ii) iliofemoral acquisitions. [19]

More recent studies however, have demonstrated substantial reduction of contrast agent administration using 128-slice dual-source CCTA with the high-pitch spiral scan mode. [20–22] These studies demonstrate that contrast agent injection can be minimized to 40–60 mL, providing acceptable image quality for the heart and of the entire aorta of TAVI candidates. However, only the minority of centers performing TAVI have the latest dual-source generation scanners available. Thus, single source CT scanners are most frequently used in everyday practice for the evaluation of patients considered for TAVI procedures. In addition, comparisons between retrospective and

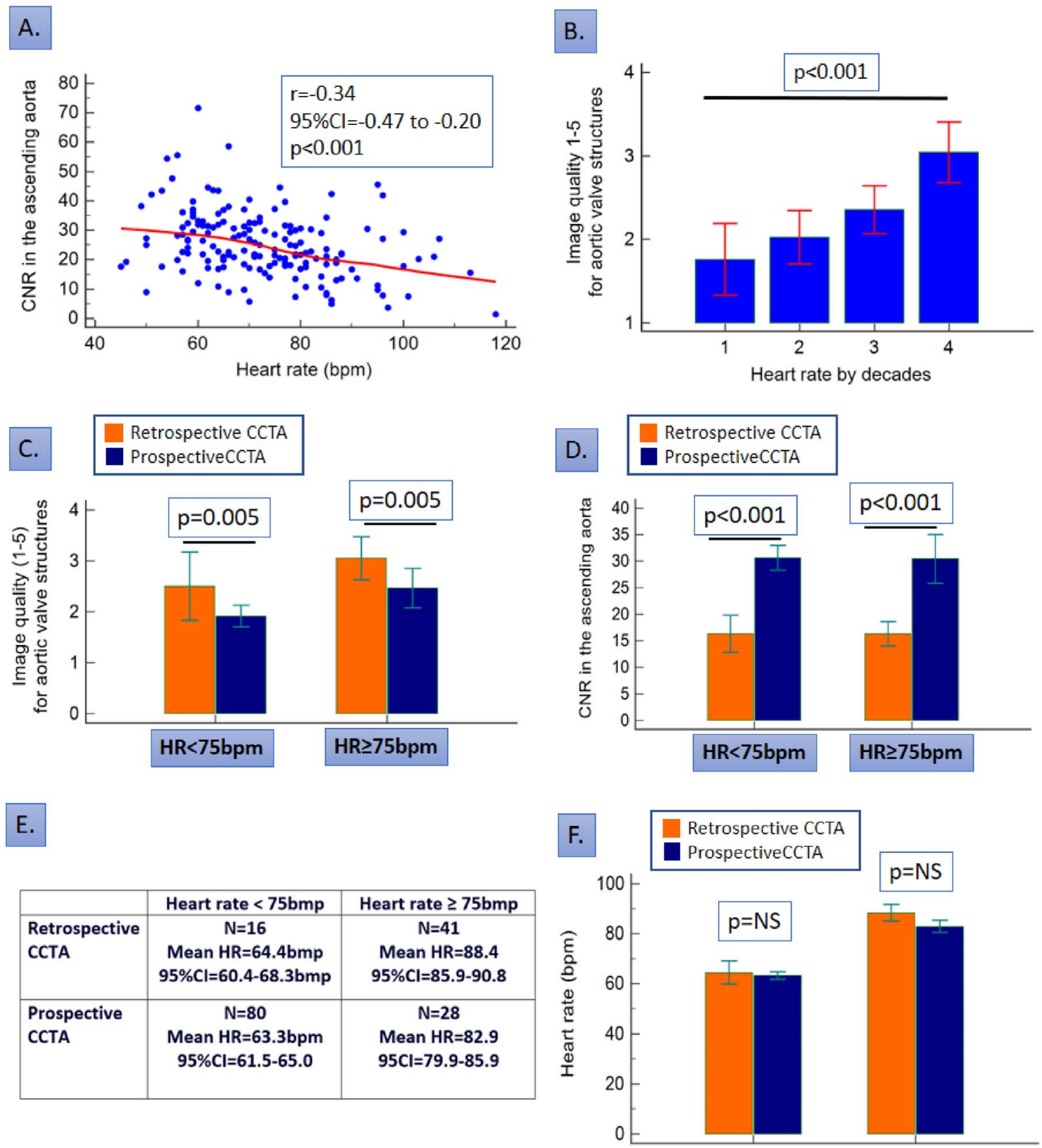

Fig. 6. Analysis by heart rate, demonstrated that CNR in the ascending aorta and image quality for the evaluation of aortic valve structures decreased with increasing heart rates (A-B). Analysis by heart rate groups showed that both image quality and CNR were significantly higher in patients prospective versus retrospective CCTA both in patients with heart rate < 75bpm and in those with heart rate ≥75bpm (C-D). 16 (28.1%) patients who underwent retrospective CCTA exhibited heart rates < 75bmp, whereas 28 (26.0%) patients who underwent prospective CCTA exhibited heart rates ≥75bpm (E). Patients within the heart rate subgroups < 75bmp and ≥75bpm showed similar heart rates irrespectively of retro- or prospective scan modes (F).

prospective CCTA protocols are to our knowledge not available at this time with single source scanners.

4.2. Our results

In our study, we demonstrated that optimization of CCTA scans using a single source scanner is more complex, but technically feasible. We systematically analyzed 165 consecutive patients considered for TAVI who underwent either a retrospectively ECG-gated (n = 57) or a prospectively ECG-triggered protocol (n=108). The resultant images were judged in terms of radiation and contrast agent exposure, visual and quantitative image quality. Prospective scans were performed with significantly lower contrast agent administration compared to the retrospective group of patients (71 mL versus 91 mL, $p < 0.01$). Hereby, it should be noted that contrast agent dose was optimized for each scan individually in previous scans, and led to diagnostic image quality in all patients included in our study. Thus, none of scans needed to be repeated due to non-diagnostic image quality. In addition, radiation exposure was substantially lower in the prospective group of patients, especially in those who underwent BMI-adapted CCTA acquisitions. However, it should be noted that radiation exposure does not represent a major issue of concern in this patient population due to the mean age of more than 80 years. The analysis of visual image quality demonstrated that prospective scans offered higher image quality for the evaluation of aortic valve structures and non-inferior image quality for the iliofemoral arteries. In the same line, quantitative analysis showed higher contrast density in the ascending and in the abdominal aorta for prospective versus retrospective scans. In addition, SNR and CNR were higher for prospective scans in the ascending aorta, whereas in the abdominal aorta prospective scans exhibited a trend for higher CNR, which albeit did not reach statistical significance.

For the evaluation of aortic valve structures, image quality was dependent on the heart rate of the patients during acquisitions, which has already been reported in previous studies. Hereby, some bias needs to be acknowledged in our study, because prospective scans were performed in patients with heart rates < 75bpm, while retrospective scans were performed in patients with heart rates ≥75Nbpm. However, CCTA examinations were acquired within a substantially larger heart rate range than initially anticipated, due to vegetative alterations during contrast agent injection and valsalva maneuver. Therefore, patients who underwent prospective CCTA exhibited a heart rate range between 46 and 96bpm, whereas patients who underwent retrospective CCTA had a heart rate range between 60 and 118bpm. This gave us the opportunity to perform subsection analysis for image quality and CNR in patients with heart rates < 75 bpm versus ≥75bpm. In fact, 16 (28.1%) patients who underwent retrospective CCTA had heart rates < 75 bmp, whereas 28 (26.0%) patients who underwent prospective CCTA exhibited had rates ≥75bpm. This enabled the comparison in terms of image quality between retro- and prospective scans. Interestingly, this analysis showed that prospective scans exhibit superior image quality and CNR compared to retrospective CCTA, both in the subgroups of patients with heart rates < 75bpm and in those with heart rate ≥75bpm. This may of course be attributed to the fact that we a priori decided to perform retrospective CCTA in patients with different heart rates, which is a well-recognized predictor of image quality with cardiac CT scans in previous studies and was confirmed by our results. [10,11,15,17] Thus, although we had the opportunity to compare prospective and retrospective scans with similar heart rates due to some alterations of heart rate during the scans, the generation of such subgroups was not based on a priori randomisation and may contain selection biases. In this regard, even with our subsection analysis a non-significant trend was noted for higher heart rates with retrospective CCTA within the subgroup of patients with heart rates ≥75bpm (Fig. 6e), which may partially explain better image quality with prospective scans. Furthermore, contrast density in the ascending and in the abdominal aorta, which is another variable of image quality was significantly higher with prospective versus retrospective scans. [10,11,15,17] This may be attributed to better timing of the contrast agent injection with prospective scans, which in contrast to the retrospective scan mode did not require a time delay between image acquisitions of the heart and of the iliofemoral arteries.

4.3. Limitations

Our study has some limitations. The number of patients included in our study was relatively small, especially for patients undergoing retrospective CCTA. In addition, patients did not randomly undergo prospective versus retrospective CCTA, but were assigned by their heart rate before the CCTA procedure. With these different protocols, different contrast agent volumes were used to reach optimal image quality for each scan mode separately, which generates some bias and potential confounders while interpreting our results. However, due to variations between the heart rate prior and during the scan, a higher range of heart rates was available for analysis, which enabled the comparison of the two protocols in patients with heart rates < 75bpm and ≥75bpm. Furthermore, a high pitch acquisition mode was not available with our scanner. Such protocols have enabled the assessment of aortic valve and iliofemoral anatomy with substantially lower contrast agent injections and simultaneously maintained image quality. However, our results may be applicable for most cardiac centers performing cardiac CT prior to TAVI, which still do not have the latest dual-source generation scanners available.

5. Conclusions

In patients scheduled for TAVI, prospective protocols require significantly lower amount of contrast agents and are simultaneously associated with lower radiation exposure, higher image quality, SNR and CNR, irrespective of the patient heart rate. This should be the preferred acquisition mode for the evaluation of both, aortic valve structures and iliofemoral anatomy, in patients considered for TAVI evaluation and if latest dual-source generation scanners are not available.

Conflict of interest

No conflict of interest to declare.

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