Supplementary data:

Table S1 Coronary CTA Acquisition Characteristics According to the Downstream Testing Strategy

|                      | Total (n=414) | FFRCT (n=195) | No FFRCT (n=160) | ICA or MPI* (n=59) | p Valueb |
|----------------------|--------------|--------------|------------------|-------------------|----------|
| Betablockers or Ivabradine | 335 (81)     | 152 (78)     | 136 (85)         | 47 (80)           | 0.10     |
| Mean heart rate, bpm  | 59 ± 12      | 57 ± 8       | 59 ± 14          | 63 ± 15           | 0.90     |
| Sinus rhythm at CTA   | 399 (96)     | 191 (98)     | 150 (94)         | 58 (98)           | 0.06     |
| Contrast, mL          | 66 ± 13      | 68 ± 16      | 64 ± 8           | 64 ± 10           | 0.01     |
| Mean diagnostic radiation dose exposure, mSv | 3.7 ± 2.3  | 3.9 ± 2.5    | 3.5 ± 2.1        | 3.6 ± 1.8         | 0.35     |

Values are mean ± SD or numbers (%). aPatients referred directly to ICA (n=58) or MPI (n=1) without FFRCT. bComparison between the groups of FFRCT and no FFRCT. CTA= computed tomography angiography; FFRCT = CT derived fractional flow reserve; ICA = invasive coronary angiography; MPI = myocardial perfusion imaging.

Table S2 FFRCT Values in Patients with Simple or Complex LMCAD

|                      | FFRCT predistal LM | FFRCT proximal LAD | FFRCT distal LAD | p Valuea | FFRCT proximal LCx | FFRCT distal LCx | p Valueb |
|----------------------|-------------------|--------------------|------------------|----------|--------------------|------------------|----------|
| Simple LMCAD with LM stenosis 1-49% | 0.97 (0.95-0.98, 0.87-0.99) | 0.94 (0.93-0.96, 0.89-0.99) | 0.84 (0.80-0.90, 0.50-0.91) | < 0.001 | 0.97 (0.94-0.98, 0.89-0.99) | 0.91 (0.89-0.93, 0.77-0.94) | < 0.001 |
|                      | n=13              | n=13               | n=13             |          | n=13              | n=13             |          |
| Simple LMCAD with LM stenosis 50-99% | 0.91 (0.82-0.95, 0.70-0.98) | 0.89 (0.80-0.94, 0.67-0.95) | 0.78 (0.69-0.89, 0.62-0.91) | < 0.001 | 0.92 (0.82-0.94, 0.67-0.97) | 0.87 (0.78-0.93, 0.61-0.94) | 0.003 |
|                      | n=8               | n=8                | n=8              |          | n=8               | n=8              |          |
| Complex LMCAD with LM stenosis 1-49% | 0.97 (0.95-0.98, 0.73-1.00) | 0.94 (0.91-0.96, 0.72-0.98) | 0.81 (0.75-0.85, 0.50-0.95) | < 0.001 | 0.95 (0.92-0.97, 0.74-0.99) | 0.87 (0.81-0.92, 0.51-0.96) | < 0.001 |
|                      | n=163             | n=98               | n=94             |          | n=133             | n=133            |          |
| Complex LMCAD with LM stenosis 50-99% | 0.91 (0.85-0.95, 0.82-0.98) | 0.86 (0.81-0.96) | 0.63 | 0.10 | 0.88 (0.85-0.96, 0.81-0.96) | 0.79 (0.77-0.94, 0.77-0.95) | 0.005 |
|                      | n=11              | n=3                | n=3              |          | n=7               | n=7              |          |

Values are median (interquartile range, range). Numbers in columns do not sum up to the total number of patients in each column header because in patients with complex LMCAD (LMCAD with one or more significant ≥50% stenosis in non-LM coronary arteries), downstream FFRCT values were registered only in segments without stenosis ≥50%. In patients with stenosis ≥50% in the proximal part of LAD or LCx, FFRCT was only registered in the non-diseased vessel. cComparison between the groups of FFRCT distal LM, FFRCT proximal LAD and FFRCT distal LAD. dComparison between the groups of FFRCT distal LM, FFRCT proximal LCx and FFRCT distal LCx. LMCAD = Left main coronary artery disease, FFRCT = CT derived fractional flow reserve. LM = Left main coronary artery; LAD = left anterior descending artery; LCx = left circumflex artery.
**Table S3** Patients with a Significant FFR<sub>CT</sub> Value According to LM Stenosis Severity and The FFR<sub>CT</sub> reading point

| Stenosis severity | 1-24% (n=104) | 25-49% (n=72) | 50-69% (n=17) | 70-99% (n=2) |
|-------------------|---------------|---------------|---------------|--------------|
| FFR<sub>CT</sub> distal LM ≤0.80 | 0 | 2 (3) | 1 (6) | 0 |
| FFR<sub>CT</sub> proximal LAD ≤0.80 | 0 | 3 (4) | 3 (18) | 0 |
| FFR<sub>CT</sub> distal LAD ≤0.80 | 32 (31) | 19 (26) | 5 (30) | 2 (100) |
| FFR<sub>CT</sub> proximal LCx ≤0.80 | 0 | 4 (6) | 1 (6) | 0 |
| FFR<sub>CT</sub> distal LCx ≤0.80 | 11 (11) | 17 (24) | 6 (35) | 1 (50) |

Values are numbers (%). Numbers in columns do not sum up to the total number of patients in each column header because in patients with complex LMCAD (LMCAD with one or more significant ≥50% stenosis in non-LM coronary arteries), downstream FFR<sub>CT</sub> values were registered only in segments without stenosis ≥50%. In patients with stenosis ≥50% in the proximal part of LAD or LCx, FFR<sub>CT</sub> was only registered in the non-diseased vessel. FFR<sub>CT</sub> = CT derived fractional flow reserve; LM = left main coronary artery; prox. = proximal; LAD = left anterior descending artery; LCx = left circumflex artery.

**Table S4** Clinical Endpoints in the FFR<sub>CT</sub> Group versus the No FFR<sub>CT</sub> Group

|                      | Total (n=414) | FFR<sub>CT</sub> (n=195) | No FFR<sub>CT</sub> (n=160) | ICA or MPI* (n=59) | p Value<sup>b</sup> |
|----------------------|---------------|--------------------------|--------------------------|-------------------|-----------------|
| Composite endpoint   |               |                          |                          |                   | 0.15            |
| All-cause death      | 17 (4)        | 9 (5)                    | 1 (1)                    | 7 (12)            | 0.71            |
| Myocardial infarction| 6 (1)         | 3 (2)                    | 1 (1)                    | 2 (3)             | --              |
| Unplanned revascularization | 7 (2) | 3 (2) | 0 | 4 (7) | -- |
| Total number of revascularizations | 44 (75) | 52 (27) | 0 | < 0.001 |

Values are numbers (%). *Patients referred directly to ICA (n=55) or MPI (n=4) without FFR<sub>CT</sub>. *Comparison between the FFR<sub>CT</sub> and No FFR<sub>CT</sub> group. ICA = invasive coronary angiography. FFR<sub>CT</sub> = CT derived fractional flow reserve. MPI = myocardial perfusion imaging.

**Table S5** Clinical Adverse Events According to FFR<sub>CT</sub> Results in the Distal Coronary Segments

|                  | distal FFR<sub>CT</sub> values ≤0.80 (n=126) | distal FFR<sub>CT</sub> values >0.80 (n=69) | p Value<sup>c</sup> |
|------------------|---------------------------------------------|---------------------------------------------|-------------------|
| Composite endpoint| 7 (6)                                       | 2 (3)                                       | 0.09             |
| All-cause death  | 2 (2)                                       | 1 (1)                                       | 0.71             |
| Myocardial infarction | 3 (2)                           | 0                                           | 0.55             |
| Unplanned revascularization | 2 (2) | 1 (1) | 1.00 |

Values are n (%). *Comparison between the groups of distal FFR<sub>CT</sub> values ≤0.80 and >0.80. FFR<sub>CT</sub> = Coronary CTA-derived fractional flow reserve; ICA = invasive coronary angiography.
**Fig. S1** FFR<sub>CT</sub> Values in Patients with LM Disease According to the Downstream Management Strategy (ICA and Revascularization)

Values are median (range). No ICA = no invasive coronary angiography, ICA = invasive coronary angiography, No Revasc = No revascularization, Revasc = revascularization.

**Fig. S2** Clinical Adverse Events as a Function of the FFR<sub>CT</sub> Values in the Distal Coronary Segments

**FFR<sub>CT</sub>** = CT derived fractional flow reserve. Composite Endpoint = all-cause death, myocardial infarction, unplanned revascularization. Distal FFR<sub>CT</sub> values = distal LAD and/or LCx values.