Table 4: Radiologic evolution after transarterial chemoembolization (TACE).

| Variable | *n* |
|---|---|
| Tumor size (%) | |
| Reduction >5 mm | 13 (43) |
| Stability +/−5 mm | 6 (20) |
| Progression >5 mm | 5 (17) |
| Unknown* | 6 (20) |
| New lesions (%) | |
| No | 15 (50) |
| Yes | 9 (30) |
| Unknown* | 6 (20) |
| Overall response (%) | |
| Regression (size reduction >5 mm and no new lesions) | 10 (33) |
| Stability (size stability +/−5 mm and no new lesions) | 4 (13) |
| Progression (size progression and/or new lesions) | 10 (33) |
| Unknown | 6 (20) |
| Downstaging (6 patients) | |
| Yes | 3 (50) |
| No | 3 (50) |

* These patients did not have imaging after TACE before transplantation.

Table 5: Orthotopic liver transplantation.

| Variable | *n* |
|---|---|
| Patients with OLT/Patients listed for OLT | 26/30 |
| Mean waiting time in days (range) | 110 (4–460) |
| Milan at transplantation (%) | |
| In | 22 (85) |
| Out | 4 |
| Progression beyond Milan criteria | 2 |
| Failed downstaging within Milan criteria | 2 |

criteria but 4 patients (15%) exceeded Milan criteria; tumor growth from within to beyond Milan criteria after being listed was observed in 2 patients, downstaging failed in 2 others. These patients were transplanted despite being beyond Milan criteria either because the tumor was at the margin of the criteria or because of uncertainty about the malignant nature of some nodules.

*3.8. Pathology of Explanted Livers.* The histopathologic analysis of the 26 explanted livers showed complete tumoral necrosis in 10 cases (42%) and partial necrosis in 15 cases (48%). The mean Edmondson score of patients with viable cancer was 2,5/4. Microvascular invasion was observed in 3 cases and macrovascular invasion in one patient. In the patients transplanted exceeding Milan criteria just before OLT (4 cases), 1 had complete tumoral necrosis (a successful downstaging attempt) and 3 patients (75%) had HCC that remained outside Milan criteria at pathological analysis.

In the 10 livers where complete HCC necrosis was observed, 9 were within Milan before transplantation. Seven patients had a regression of the tumor following TACE, 2 had stable lesions, and 1 had new lesions identified.

Table 6: Characteristics of patients with and without cancer recurrence after OLT (mean follow-up 56 months; range: 6–142 months).

| | No cancer recurrence | Cancer recurrence | *P** |
|---|---|---|---|
| *n* | 21 | 5 | |
| Tumor response to TACE | | | |
| regression/stability (%) | 15 (71) | 0 | .051 |
| Progression | 2 (10) | 4 (80) | |
| Not evaluated | 4 (19) | 1 (20) | |
| Milan criteria before OLT (%) | | | |
| within Milan | 19 (90) | 3 (60) | .1548 |
| outside Milan | 2 (10) | 2 (40) | |
| Pathological tumor analysis (%) | | | |
| complete necrosis | 10 (48) | 0 | .066 |
| microscopic invasion | 0 | 3 (60) | .004 |
| Mortality | 2 (10) | 4 (80) | .002 |

* One sided *P*-values calculated using the Fisher exact test.

*3.9. Follow-Up.* Table 6 summarizes patients' characteristics after OLT with a mean follow-up of 56 months (range: 6–142 months). At follow-up, we identified 21 patients (81%) without cancer recurrence and 5 with cancer recurrence (19%). In patients identified with cancer recurrence, 3 (60%) had cancer in the transplanted liver and 2 (40%) had lung metastasis. Mean time to recurrence was 13.8 months (range 6–22 months).

Patients without cancer recurrence had more tumoral regression/stability after TACE than patients with cancer recurrence (71% versus 0%; $P = .051$). In addition, patients with no tumoral recurrence were almost all within Milan criteria before transplantation (90%) as opposed to patients with tumoral recurrence (60%). Therefore, Milan status was associated to a relative risk of cancer recurrence posttransplantation of 6.33 with a 95% CI (1.53–26.18). Patients with no cancer recurrence showed more complete necrosis (48% versus 0%; $P = .066$) and significantly less microscopic invasion (0% versus 60%; $P = .004$) on pathological analysis.

Six patients died (23%) at follow-up: 1 from postoperative complications, 4 from cancer recurrence, and 1 from cirrhosis associated with hepatitis C 7 years posttransplantation (Figure 1). Therefore, survival of patients with tumor recurrence was poor, mortality was significantly lower in patients without cancer recurrence compared to patients with cancer recurrence (10% versus 80%; $P = .002$).

*3.10. Subgroup Analysis according to Milan Status.* In the 4 patients that exceeded Milan criteria before transplantation, 2 represented a failed attempt at downstaging and cancer progression was observed in 2. Three of the 4 patients (75%) exceeding Milan at OLT had HCC discovered at histology. At follow-up, HCC recurrence was observed in 2 of these patients (50%). Hence, being outside Milan before OLT significantly increased risk of cancer recurrence after OLT (RR: 6.33, 95% CI: 1.53–26.18).

In the 22 patients within Milan criteria before transplantation, 10 (45%) had complete HCC necrosis and all