**Table 1:** Definitions of Initial Poor Function (IPF) and Primary Non Function (PNF) found in the literature. Table freely extracted from Olthoff et al.[121], Chen XB et al.[18] and Pareja et al.[152]). The mentioned studies are cited in chronological order.

|  |  |  |
| --- | --- | --- |
| Reference | IPF | PNF |
| Makowka et al.[153]  1987 | On POD1:   * AST > 3500 IU/L * ALT > 2500 IU/L * PT > 25 s |  |
| Greig et al.[154]  1990 | On POD2-7:   * AST > 2500 IU/L |  |
| Mor et al.[155]  1992 | On POD1   * AST or ALT > 2000 IU/L |  |
| Ploeg et al.[156]  1993 | On POD2-7:   * AST > 2000 IU/L * PT > 16 sec * NH4 > 50 μmol/L | * Not-life sustaining graft leading to retransplantationor death within POD7 |
| Strasberg et al.[157]  1994 | On POD1-7:   * AST > 1500 IU/L * PT > 20 s |  |
| Gonzalez et al.[114]  1994 | On POD1-3, final score 7-9 measuring:   * ALT > 2500 IU/L * PT < 60 s despite FFP * Bile output < 40 mL/d |  |
| Takaya et al.[158]  1995 |  | * Not-life sustaining graft within POD14, together with either:   + coagulopathy   + failed awake   + renal dysfunction   + insufficient bile production   + lactic acidosis   + haemodynamic instability |
| Maring et al.[84]  1997 | On POD 2-7:   * AST > 2500 IU/L * PT > 16 s * NH4 > 50 μmol/L |  |
| Deschènes et al.[115]  1998 | On POD1-7:   * Bilirubin > 10 mg/dL * PT > 7 s * Encephalopathy |  |
| Pokorny et al.[159]  2000 | * AST > 2500 IU/L * clotting factor support > 2 days * bile output < 20 mL/d |  |
| Broering et al.[160]  2002 | * ALT or AST or GDH > 2000 IU/L * FFP substituted for > 5 days postoperatively | * Not-life sustaining graft leading to retransplantation or death within POD10 |
| Nanashima et al.[161]  2002 | Two consecutive meaurements within POD3:   * ALT or AST > 1500 IU/L | * IPF-induced retransplantation or death |
| Heise et al.[162]  2003 | * Scoring system based on ALT, AST, bile output,  Prothrombin activity on POD1-3-7-14  (Berlin score ranging from 4 to 8) Berlin C (IPF): 7-8 |  |
| Tekin et al.[163]  2004 | On POD7:   * AST > 1500 IU/L   and   * PT > 20 s | * Not-life sustaining graft leading to retransplantationor death within POD7 |
| Ben Ari et al.[164]  2004 | * AST or ALT > 2000 IU/L on POD2 * INR > 1.6 on POD2-10 * Bilirubin > 10 mg/dL on POD2-10 | * Not-life sustaining graft leading to retransplantationor death within POD10 |
| Kremers et al.[165]  2004 |  | * ALT > 2500 IU/L * Glucose < 60 mg/dL * INR > 2.5 * bile flow < 50 mL/d |
| Pokorny et al.[166]  2005 | On POD5:   * AST > 2500 IU/L   or   * clotting support > 2 d | * Not-life sustaining graft leading to retransplantationor death within POD7 |
| Monbaliu et al.[167]  2008 |  | * Persisting encephalopathy * Irreversible metabolic acidosis * Profound hypoglicaemia * Severe coagulopathy * Insufficient bile production * Increased AST |
| Cieslak et al.[168]  2009 | Within POD1-7   * AST or ALT > 2500 IU/L   or   * Prothrombin index < 50% |  |
| Dhillon et al.[169]  2010 | * [(AST+ALT)/2] on POD2:   + <285 IU/L: good function   + 285-986 IU/L: average function   + >986 IU/L: IPF | * IPF-induced retransplantationor death within POD7 |
| Nemes et al.[170]  2010 | On POD5:   * [Serum bilirubin (μmol/L)]/[Prothrombin (%)] > 1 |  |
| Olthoff et al.[121]  2010 | On POD1-7, one within:   * Bilirubin ≥ 10 mg/dL on POD7 * INR ≥ 1.6 on POD7 * ALT or AST > 2000 IU/L within POD7 |  |
| Lock et al.[88,87]  2010 | Two LiMax readouts during the first 24 hours:   * LiMax = 60-120 μg/kg/h | * Two LiMax readouts during the first 24 hours: LiMax < 60 μg/kg/h |
| Mathé et al.[171]  2011 | Two consecutive measurements within POD3:   * ALT or AST > 1500 IU/L | * IPF-induced retransplantation or death |

**Legend:** ALT = Alanine – Aminotransferase, AST = Aspartate – Aminotransferase, FFP = Fresh Free Plasma, GDH = Glutamate Dehydrogenase, INR = International Normalised Ratio, LiMax = Liver Maximal Function Capacity, POD = postoperative day, PT = Prothrombin time.

**Table 2:** studies overview. As noticeable, for the majority of the markers just very few studies are available about their direct application specifically to LT. Where more than one study was present for a specific technique, chronological order has been adopted.

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Thecnique | Study | Type (P/R) | Primary end-point: | Sample | POD | Cut-off value: | AUROC (95%CI) | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) |
| ICG-PDR | Olmedilla et al.[65]  2009 | P | EAD prediction | 172 LT:  31.9% HCC, 29.6% viral, 23.8% alcoholic | 1 | 10%/min | 0.967 (0.915-0991) | 100 (69-100) | 90.4 (84.7-94.6) | 40 | 100 |
|  | Levesque et al.[71]  2009 | P | EAD prediction | 72 LT (including LDLT) | 0-5 | 12.85%/min |  | 90 | 97 |  |  |
|  | Schneider et al.[72]  2011 | P | Graft loss or patient death on POD30 | 86 LT:  36% viral, 29% alcoholic | 7 | 12.3%/min | 0.729 (0.608-0.850) | 69 | 67 | 57 | 77 |
| Pre-operative MELD + postoperative ICG-PDR | Klinzing et al.[74]  2014 | P | ICU-LOS, mortality | 50 LT | 0 (<6 h after ICU admission) | MELD > 25,  ICG-PDR < 20%/min | 0.79 | 100 | 59 |  |  |
| ICG-PDR + INR | Olmedilla et al.[73]  2015 | P | 1-month mortality or need for retransplantation within POD7 | 332 LT (+77 validations) | 1 | ICG-PDR < 10%/min,  INR > 2.2 | 0.76 (0.66-0.86) | 48 (31-66) | 95 (91-97) | 50 (32-68) | 94 (91-96) |
| LiMax | Lock et al.[51]  2010 | P | EAD requiring reintervention before POD2 or causing death/retransplantation within POD14 | 99 LT:  32% alcoholic, 23% HCV | 0  1 | 64 μg/kg/h  43 μg/kg/h | 0.960 (0.921-0.998)  0.992 (0.975-1.000) | 100 (60-100)  100 (31-100) | 92 (84-97)  100 (94-100) | 53 (27-78)  100(31-100) | 100 (95-100)  100 (94-100) |
| Platelets count | Lesurtel et al.[107]  2014 | R | Severe complications or 3-months mortality | 257 LT:  38% HCV | 5 | 60x109/L |  | 58 | 61 |  |  |
|  | Li et al.[108]  2015 | R | EAD prediction | 234 LDLT:  45% HCC | 2 | 68x109/L | 0.678 | 73 | 59 |  |  |
| Factor V | Zulian et al.[172]  2015 | R | Graft failure within POD90 | 105 LT:  79.5% HCC, 76.2% HCV | 2 | 41.5% | 0.65 | 42.9 | 87.9 | 35.3 | 90.9 |
| AST | Robertson et al.[116]  2015 | P | Graft loss at POD90 | 1091 LT:  22% HCV | 3 | 2 cut-offs: 106.5 IU and 2744.5 IU | 0.739 (0.663-0.814) |  |  | 34.62 | 99.45 |
| Bilirubin | Wagener et al.[120]  2013 | R | Graft loss or death within POD90 | 572 LT:  51.9% HCV | 2 | 6.55 mg/dL | 0.809 (0.742-0.877) | 72.5 | 70.4 |  |  |
| Bilirubin, INR and transaminases | Olthoff et al.[121]  2010 | R | EAD definition to predict mortality and graft loss | 300 LT | 7 | Bilirubin > 10 mg/dL, INR > 1.6, ALT or AST > 2000 IU/mL | 0.75-0.78 |  |  |  |  |
| Lactates | Wu et al.[124]  2011 | P | EAD prediction | 222 LT:  50% HBV, 41% HCC | 1 | 24.8% | 0.961 (0.948-0.974) | 95.5 | 88.9 |  |  |
| IGF-1 | Bassanello et al.[127]  2004 | P | Explore GH/IGF-1 axis changes during the perioperative course of LT | 15 LT:  52% viral, 20% alcoholic | 7 | n.a |  |  |  |  |  |
|  | Salso et al.[130]  2014 | R | 90-days patient survival | 30 LT:  40% HCV, 20% HBV | 15 | 90 mUI/mL | 0.92 | 86 | 87 |  |  |
|  | Nicolini et al.[128]  2015 | P | 3-years actual survival | 31 LT:  42.5% HCV | 15 | Normal values classified according to Immunolite 2000® system reference-ranges |  |  |  |  |  |
| MELD | Wagener et al.[120]  2013 | R | Graft loss or mortality within POD90 | 572 LT:  51.9% HCV | 5 | ≥19 | 0.812 (0.739-0.886) |  |  |  |  |
|  | Toshima et al.[131]  2014 | R | Graft loss or mortality within POD180 | 217 LDLT:  47.9% HCV | 2  7 | ≥19 | 0.779  0.933 | 68.2  100 | 79.5  74.9 | 27.3  31.0 | 95.7  100 |
| MELD lactate | Cardoso et al.[132]  2014 | P | Mortality within POD30 | 58 LT:  43% HCV, 26% alcoholic | 1 hour after surgery | 26.3 | 0.80 |  |  |  |  |
| APACHE IV | Hu et al.[140]  2013 | R | Mortality | 195 LT | 1 | ≥55.5 | 0.937 (0.892-0.981) | 85.2 | 91.1 | 60.5 | 97.5 |
| SOFA | Wong et al.[147]  2010 | R | 3-months mortality | 149 LT:  53% HBV | 7 | ≥8 | 0.953 (0.902-1.000) | 95 | 91 |  |  |
| CLIF-SOFA | Pan et al.[150]  2014 | R | 1-year mortality | 323 LT:  62% HBV, 27% hepatoma, 26% HCV | 3  7 | >8 | 0.808 (0.729-0.888)  0.877 (0.813-0.941) | 67  64 | 87  95 |  |  |
| MEAF | Pareja et al.[152]  2015 | R | EAD definition ti predict 3-months mortality | 874 LT (+200 validation) | 3 | >8 |  |  |  |  |  |

Type P = Prospective, Type R = Retrospective, POD = postoperative day in which best discriminating values were detected, PPV = Positive Predictive Value, NPV = Negative Predictive Value, 95%CI = 95% Confidence Interval, LT = Liver Transplant, LDLT = Living Donor Liver Transplant, HCV = Hepatitis C Virus, HBV = Hepatitis B Virus, HCC = Hepatocellular Carcinoma, Sample: only specified if a disease accounts for more than 20% of the overall sample.