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| **Supplementary Table 1. Detailed search strategy** | |  |
| **Search from Pubmed Database** | | |
| No. | Keywords | Results |
| #1 | "liver cirrhosis"[MeSH Terms] OR "liver diseases"[MeSH Terms] OR "hepatic encephalopathy"[MeSH Terms] OR "liver failure"[MeSH Terms] | 559,337 |
| #2 | "liver fibrosis"[Title/Abstract] OR "liver cirrho\*"[Title/Abstract] OR "cirrho\*"[Title/Abstract] OR "liver dysfunction\*"[Title/Abstract] OR "liver disease\*"[Title/Abstract] OR "liver failure\*"[Title/Abstract] OR "hepatic fibrosis"[Title/Abstract] OR "hepatic disease\*"[Title/Abstract] OR "hepatic dysfunction\*"[Title/Abstract] OR "hepatic cirrho\*"[Title/Abstract] OR "hepatic failure\*"[Title/Abstract] OR "liver encephalopath\*"[Title/Abstract] OR "hepatic encephalopath\*"[Title/Abstract] OR "portal systemic encephalopath\*"[Title/Abstract] OR "hepatocerebral encephalopath\*"[Title/Abstract] OR "portosystemic encephalopath\*"[Title/Abstract] OR "hepatic coma\*"[Title/Abstract] OR "hepatic stupor\*"[Title/Abstract] | 232,069 |
| #3 | 1 OR 2 | 624,115 |
| #4 | "amino acids, branched chain"[MeSH Terms] | 49,994 |
| #5 | "branched chain amino acid\*"[Title/Abstract] OR "amino acids branched chain"[Title/Abstract] OR "BCAA"[Title/Abstract] | 6,732 |
| #6 | 4 OR 5 | 53,622 |
| #7 | 3 AND 6 | 1,830 |
| **Total** | | **166** |
|  |  |  |
| **Search from Embase Database** | | |
| No. | Keywords | Results |
| #1 | liver cirrhosis'/exp OR 'liver disease'/exp OR 'hepatic encephalopathy'/exp OR 'liver failure'/exp OR 'liver fibrosis'/exp OR 'liver dysfunction'/exp OR 'hepatic coma'/exp | 1,077,900 |
| #2 | liver fibrosis':ab,ti OR 'liver cirrho\*':ab,ti OR 'cirrho\*':ab,ti OR 'liver dysfunction\*':ab,ti OR 'liver disease\*':ab,ti OR 'liver failure\*':ab,ti OR 'hepatic fibrosis':ab,ti OR 'hepatic disease\*':ab,ti OR 'hepatic dysfunction\*':ab,ti OR 'hepatic cirrho\*':ab,ti OR 'hepatic failure\*':ab,ti OR 'liver encephalopath\*':ab,ti OR 'hepatic encephalopath\*':ab,ti OR 'portal-systemic encephalopath\*':ab,ti OR 'hepatocerebral encephalopath\*':ab,ti OR 'portosystemic encephalopath\*':ab,ti OR 'hepatic coma\*':ab,ti OR 'hepatic stupor\*':ab,ti | 343,750 |
| #3 | 1 OR 2 | 1,110,346 |
| #4 | branched chain amino acid'/exp | 74,406 |
| #5 | branched-chain amino acid\*':ab,ti OR 'amino acids, branched-chain':ab,ti OR bcaa:ab,ti | 8,190 |
| #6 | 4 OR 5 | 77,201 |
| #7 | 3 AND 6 | 3,571 |
| **Total** | | **291** |
|  |  |  |
| **Search from Cochrane Library Database** | | |
| No. | Keywords | Results |
| #1 | MeSH descriptor: [Liver Cirrhosis] OR MeSH descriptor: [Liver Diseases] explode all trees OR MeSH descriptor: [Hepatic Encephalopathy] explode all trees OR MeSH descriptor: [Liver Failure] explode all trees | 15,176 |
| #2 | (Liver fibrosis):ti,ab,kw OR (Liver cirrho\*):ti,ab,kw OR (Cirrho\*):ti,ab,kw OR (Liver dysfunction\*):ti,ab,kw OR (Liver disease\*):ti,ab,kw OR (Liver failure\*):ti,ab,kw OR (Hepatic fibrosis):ti,ab,kw OR (Hepatic disease\*):ti,ab,kw OR (Hepatic dysfunction\*):ti,ab,kw OR (Hepatic cirrho\*):ti,ab,kw OR (Hepatic failure\*):ti,ab,kw OR (Liver encephalopath\*):ti,ab,kw OR (Hepatic encephalopath\*):ti,ab,kw OR (Portal-systemic encephalopath\*):ti,ab,kw OR (Hepatocerebral encephalopath\*):ti,ab,kw OR (Portosystemic encephalopath\*):ti,ab,kw OR (Hepatic coma\*):ti,ab,kw OR (Hepatic stupor\*):ti,ab,kw | 37,911 |
| #3 | #1 OR #2 | 44,784 |
| #4 | MeSH descriptor: [Amino Acids, Branched-Chain] | 1,873 |
| #5 | (Branched-Chain Amino Acid\*):ti,ab,kw OR (Amino Acids, Branched-Chain):ti,ab,kw OR (BCAA):ti,ab,kw | 1,040 |
| #6 | #4 OR #5 | 2,591 |
| #7 | #3 AND #6 | 324 |
| **Total** | | **187** |

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| **Supplementary Table 2. Characteristics of studies included** | | | | | | | | | | |
| **Author (year)** | **Country** | **Study design** | **Study population** | **Control** | **No. of patients** | | **Age (mean ± SD)** | | **Male (%)** | |
| **BCAA** | **Control** | **BCAA** | **Control** | **BCAA** | **Control** |
| Horst (1984) | USA | RCT | Liver cirrhosis | Protein | 17 | 20 | 57.0 ± 9.5 | 60.0 ± 11.2 | 64.3% | 66.7% |
| Calvey (1985) | UK | RCT | Alcoholic hepatitis | Diet | 21 | 43 | 47.0 ± 9.0 | 50.5 ± 9.5 | 42.9% | 51.2% |
| Kanematsu (1988) | Japan | RCT | Resection for HCC | Conventional control | 29 | 27 | 52.0 ± 9.0 | 51.0 ± 7.0 | 72.4% | 96.3% |
| Yoshida (1989) | Japan | RCT | Resection for HCC | Diet | 20 | 20 | NA | NA | 70.0% | 70.0% |
| Nagasue (1997) | Japan | RCT | Resection for HCC | Diet | 67 | 65 | NA | NA | 80.6% | 84.6% |
| Meng (1999) | Hong Kong | RCT | Resection for HCC | Diet | 21 | 23 | 51.5 ± 10.8 | 53.3 ± 12.8 | 90.5% | 78.3% |
| Marchesini (2003) | Italy | RCT | Resection for HCC | Lactose + MDX | 58 | 115 | 59.0 ± 1.0 | 59.5 ± 1.0 | 61.0% | 64.3% |
| Poon (2004) | Hong Kong | RCT | HCC | Diet | 41 | 43 | 59.0 ± 15.0 | 59.0 ± 13.2 | 95.1% | 90.7% |
| Muto (2005) | Japan | RCT | Resection for HCC | Diet | 320 | 326 | 62.0 ± 8.0 | 61.0 ± 9.0 | 46.8% | 47.7% |
| Togo (2005) | Japan | RCT | Resection for HCC | Control | 21 | 22 | 66.5 ± 4.5 | 64.3 ± 9.1 | 81.0% | 77.3% |
| Muto (2006) | Japan | RCT | Resection for HCC | Diet | 227 | 204 | NA | NA | NA | NA |
| Kobayashi (2008) | Japan | RCT | Resection for HCC | No BCAA | 20 | 20 | 62.9 ± 5.7 | 59.5 ± 7.2 | 100.0% | 100.0% |
| Okabayashi (2008) | Japan | Retrospective cohort | Resection for HCC | Control | 40 | 72 | 68.3 ± 8.1 | 65.7 ± 8.6 | 72.5% | 76.4% |
| Kawamura (2009) | Japan | RCT | Resection for HCC | No BCAA | 27 | 23 | 62.7 ± 10.1 | 62.3 ± 7.3 | 48.1% | 52.2% |
| Ishikawa (2010) | Japan | RCT | Resection for HCC | Control | 11 | 13 | 63.1 ± 12.5 | 61.3 ± 11.3 | 54.5% | 61.5% |
| Kuroda (2010) | Japan | Prospective cohort | HCC treated by TACE | Diet | 20 | 15 | 65.6 ± 7.0 | 66.0 ± 8.1 | 65.0% | 60.0% |
| Hayaishi (2011) | Japan | Retrospective cohort | Liver cirrhosis - Child A | - | 56 | 155 | 66.0 ± 12.8 | 64.0 ± 15.8 | 41.1% | 59.4% |
| Les (2011) | Spain | RCT | Resection for HCC | MDX | 58 | 58 | 64.1 ± 10.4 | 62.5 ± 10.4 | 77.6% | 74.1% |
| Ichikawa (2013) | Japan | RCT | Resection for HCC | Control | 26 | 30 | 64.7 ± 9.8 | 64.5 ± 11.4 | 69.2% | 66.7% |
| Yoshiji (2013) | Japan | RCT | HCC | Control | 29 | 22 | 63.6 ± 15.3 | 64.3 ± 9.1 | 62.7% | 59.5% |
| Kanekawa (2014) | Japan | Retrospective cohort | Resection for HCC - Child A or B | Control | 49 | 43 | 66.3 ± 7.0 | 68.0 ± 7.0 | 87.8% | 79.1% |
| Hanai (2015) | Japan | Retrospective cohort | Resection for HCC | Diet | 94 | 36 | 66.0 ± 12.8 | 64.0 ± 15.8 | 57.4% | 61.1% |
| Kikuchi (2016) | Japan | RCT | Resection for HCC | Control | 39 | 38 | 69.4 ± 7.5 | 71.9 ± 7.4 | 79.5% | 76.3% |
| Nojiri (2017) | Japan | RCT | HCC treated by TACE and RFA | Control | 25 | 26 | 69.7 ± 9.0 | 69.1 ± 11.0 | 60.0% | 57.7% |
| Park (2017) | South Korea | Retrospective cohort | Resection for HCC | Diet | 41 | 41 | 59.0 ± 9.0 | 59.0 ± 12.0 | 78.0% | 73.2% |
| Tada (2019) | Japan | Retrospective cohort | HCC | Control | 27 | 51 | 67.0 ± 7.4 | 71.0 ± 9.3 | 59.3% | 66.7% |
| Hachiya (2020) | Japan | RCT | Resection for HCC | Control | 74 | 80 | 69.0 ± 9.5 | 70.0 ± 9.5 | 79.7% | 82.5% |
| Park (2020) | Korea | Prospective cohort | Resection for HCC | Diet | 63 | 61 | 60.0 ± 10.0 | 58.0 ± 11.0 | 71.4% | 60.7% |
| Abbreviations: SD, standard deviation; BCAA, branched-chain amino acids; USA, United States of America; UK, United Kingdom; RCT, randomized-controlled trial; HCC, hepatocellular carcinoma; NA, not available; TACE, trans-arterial chemoembolization; RFA, radiofrequency ablation; MDX, maltodextrine | | | | | | | | | | |

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| **Supplementary Table 3.** Quality assessment of the included studies | | | | | | | |
| ***Using the Risk of Bias tool (n=20)*** | | | | | | | |
| First author | Publication  Year | Type of Bias | | | | | |
| Randomisation process | Deviations from the intended interventions | Missing outcome data | Measurement of the outcome | Selection of the reported result | Overall bias |
| Horst | 1984 | Low risk | Low risk | Low risk | High risk | Low risk | Low risk |
| Calvey | 1985 | Some concerns | High risk | High risk | Low risk | Low risk | Some concerns |
| Kanematsu | 1988 | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk |
| Yoshida | 1989 | Some concerns | High risk | Low risk | Low risk | Low risk | Some concerns |
| Nagasue | 1997 | Low risk | High risk | Low risk | Low risk | Low risk | Low risk |
| Meng | 1999 | Low risk | High risk | Low risk | Low risk | Low risk | Low risk |
| Marchesini | 2003 | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk |
| Poon | 2004 | Low risk | High risk | Low risk | Low risk | Low risk | Low risk |
| Muto | 2005 | Low risk | High risk | High risk | Low risk | Low risk | Some concerns |
| Togo | 2005 | Low risk | High risk | Low risk | Low risk | Low risk | Low risk |
| Muto | 2006 | Low risk | High risk | Low risk | Low risk | Low risk | Low risk |
| Kobayashi | 2008 | Low risk | High risk | Low risk | Low risk | Low risk | Low risk |
| Kawamura | 2009 | Low risk | High risk | Low risk | Low risk | Low risk | Low risk |
| Ishikawa | 2010 | Some concerns | Low risk | Low risk | Low risk | Low risk | Low risk |
| Les | 2011 | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk |
| Ichikawa | 2013 | Some concerns | High risk | Low risk | Low risk | Low risk | Some concerns |
| Yoshiji | 2013 | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk |
| Kikuchi | 2016 | Low risk | High risk | Low risk | Low risk | Low risk | Low risk |
| Nojiri | 2017 | Low risk | High risk | Low risk | Low risk | Low risk | Low risk |
| Hachiya | 2020 | Low risk | High risk | Low risk | Some concerns | Low risk | Some concerns |
| ***Using the Risk of Bias Assessment tool for Non-randomized Studies tool (n=8)*** | | | | | | | |
|  |  | Type of Bias | | | | | |
| First author | Publication  Year | Selection of participants | Confounding variables | Measurement of exposure | Blinding of outcome assessment | Incomplete outcome data | Selective outcome reporting |
| Okabayashi | 2008 | Low risk | High risk | Low risk | Low risk | Low risk | Low risk |
| Kuroda | 2010 | Low risk | High risk | Low risk | Low risk | Low risk | Low risk |
| Hayaishi | 2011 | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk |
| Kanekawa | 2014 | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk |
| Hanai | 2015 | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk |
| Park | 2017 | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk |
| Tada | 2019 | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk |
| Park | 2020 | Low risk | High risk | Low risk | Low risk | Low risk | Low risk |

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| **Supplementary Table 4.** Summary according to the type of hepatic decompensation | | | | | | |
| Author (year) | Study design |  | Number of patients | | Number of events | |
| BCAA | Control | BCAA | Control |
| ***Ascites (n=4)*** | | | | | | |
| Poon (2004) | RCT | HCC | 41 | 43 | 3 | 10 |
| Okabayashi (2008) | Retrospective cohort | Resection for HCC | 40 | 72 | 3 | 12 |
| Park (2017) | Retrospective cohort | Resection for HCC | 41 | 41 | 10 | 9 |
| Park (2020) | Retrospective cohort | Resection for HCC | 63 | 61 | 6 | 17 |
| ***Variceal bleeding or rupture (n=5)*** | | | | | | |
| Poon (2004) | RCT | HCC | 41 | 43 | 1 | 0 |
| Muto (2005) | RCT | Resection for HCC | 314 | 308 | 8 | 9 |
| Kuroda (2010) | Prospective cohort | HCC treated by TACE | 20 | 15 | 0 | 1 |
| Park (2017) | Retrospective cohort | Resection for HCC | 41 | 41 | 9 | 3 |
| Park (2020) | Retrospective cohort | Resection for HCC | 63 | 61 | 2 | 6 |
| ***Hepatorenal syndrome or renal failure (n=3)*** | | | | | | |
| Poon (2004) | RCT | HCC | 41 | 43 | 0 | 1 |
| Park (2017) | Retrospective cohort | Resection for HCC | 41 | 41 | 4 | 2 |
| Park (2020) | Retrospective cohort | Resection for HCC | 63 | 61 | 1 | 1 |
| Abbreviations: BCAA, branched-chain amino acids; RCT, randomized-controlled trial | | | | | | |

A picture containing table

Description automatically generated

**Supplementary Figure 1. Risk of bias graph for randomized control trials using the version 2 of Risk-of-bias tool**

Diagram, table

Description automatically generated with medium confidence

**Supplementary Figure 2. Risk of bias graph for observational studies using the risk of bias assessment tool for non-randomized studies (RoBANS) tool**