INFORMATION BRIEF (RAPID REVIEW)

Transarterial Chemoembolisation for Breast Cancer

Malaysian Health Technology Assessment Section (MaHTAS)
Medical Development Division
Ministry of Health Malaysia
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Rapid Review
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TITLE: TRANSARTERIAL CHEMOEMBOLISATION (TACE) FOR BREAST CANCER

PURPOSE

To provide brief information on the effectiveness and safety of Transarterial Chemoembolisation (TACE) for Breast Cancer following request from the Director of Medical Practice Division, Ministry of Health, Malaysia.

BACKGROUND

Breast Cancer and Metastatic Breast Cancer

Breast cancer is a heterogeneous disease with distinct molecular subtypes, each associated with varying prognosis and responses to treatment. Around 50% of patients diagnosed with Breast Cancer will develop metastasis, with the liver, lungs, brain, and bones being common sites of spread. Liver metastases from breast cancer (BCLM) occur in about 50% of patients with metastatic Breast Cancer and are among the most frequent initial sites of metastasis.[1.]

Breast cancer represents a significant global health challenge. It is the most commonly diagnosed in the world with an estimated 2.3 million new cases recorded in 2020 in both sexes combined.[2] Representing a quarter of all cancer cases in females, it was by far the most commonly diagnosed cancer in women in 2020, and its burden has been growing in many parts of the world, particularly in transitioning countries. An estimated 685,000 women died from breast cancer in 2020, corresponding to 16% or one in every six cancer deaths in women. Previously insufficient public health response to this development has led to the recent launch of the Global Breast Cancer Initiative by the World Health Organization (WHO)[3].

In Malaysia, Breast cancer is the most prevalent cancer among women. According to the Malaysian National Cancer Registry Report (2017 to 2021), it accounted for 17.6% of all cancer cases among females during that period, with an age-standardised incidence rate of 38.9. per 100,000 women. Notably, 50.5% of cases were diagnosed at late stages (Stage III and IV). Ethnic disparities in breast cancer incidence have been observed in Malaysia. A study analysing data from 2017 till 2021 found that Indian women had the highest incidence rates, followed by Chinese and Malay women. In 2017 to 2021, starting at age 40, a greater incidence rate is observed compared to previous data (2012 to 2016), particularly in the 65 to 69 age group. Survival rates also vary significantly depending on the stage at diagnosis, with five years relative survival rates of 87.5% for Stage I, 80.7% for Stage II, 59.7% for Stage III and 23.3% for Stage IV. These statistics highlight the critical importance of early detection and timely treatment in improving breast cancer outcomes in Malaysia.[4]

Current management option for Breast Cancer

For non-metastatic breast cancer, the main objective of treatment is to eliminate the tumor from the breast and regional lymph nodes and to prevent metastatic recurrence. Local therapy for nonmetastatic breast cancer consists of surgical resection and sampling or removal of axillary lymph nodes, with consideration of postoperative radiation. Systemic therapy may be preoperative (neoadjuvant), postoperative (adjuvant), or both. Breast cancer subtype guides the standard systemic therapy administered, which consists of endocrine therapy for all HR+ tumors (with some patients requiring chemotherapy as well), trastuzumab-based ERBB2-directed antibody therapy plus chemotherapy for all ERBB2+ tumors (with endocrine therapy given in addition, if concurrent HR positivity), and chemotherapy alone for triple-negative breast cancer. In metastatic breast cancer, the treatment goals shift to prolonging survival and alleviating symptoms. While metastatic breast cancer remains incurable for most patients, systemic therapies similar to those used in neoadjuvant and adjuvant settings are applied. However, local treatments like surgery and radiation are typically reserved for palliative care in metastatic disease.[5]

Transarterial Chemoembolisation

Transarterial Chemoembolisation (TACE) is a catheter-based, minimally invasive therapeutic approach that combines selective chemotherapy administration with embolisation of the tumor's vascular supply. Chemotherapeutic drugs for TACE included adriamycin, doxorubicin, fluorouracil, 5-FUDR (a metabolite of 5-fluorouracil), cisplatin, oxaliplatin, mitomycin-C and gemcitabine. The embolising agent may consist of tiny microspheres, metal coils, or a specialised gel.[5] For hepatic arteries embolisation lipiodol was commonly used, other materials such as beads, starch microspheres or gelatin-sponge particles were also used.[6] This procedure is used to administer both chemotherapy and embolising agent that induces blood clotting. Embolisation blocks the tumour’s blood supply, depriving cancer cells of oxygen and nutrients, leading to their death. Transarterial chemoembolisation (TACE) delivers high-dose drugs directly into the tumour tissue via the tumour-feeding arteries, allowing for increased drug absorption by the tumor tissue.[7] The loss of blood flow from embolisation keeps chemotherapy from being washed away from around the cancer, making it more effective. Following TACE, treated tumors will often shrink significantly or even die, with no further living cancer cells remaining.[8]

Transarterial Chemoembolisation for Breast Cancer & Metastatic Breast Cancer

Transarterial Chemoembolisation was approved to treat unresectable liver tumours originated both from liver or other organs, such as breast, colon, rectum and so on. As TACE gradually develops into a mature technique and can be performed by experienced doctors, it provides a therapeutic choice for LMBC patients especially for those who cannot undertake liver resection or develop resistance for systemic chemotherapy.[7] In Liver Metastasis Breast Cancer, TACE delivers medications directly to the liver using a catheter, a small, flexible tube inserted into an artery in the groin. A specialist, typically an interventional radiologist, performs the procedure by making a small incision in the groin to insert the catheter into the femoral artery. The catheter is then guided through the aorta to the hepatic artery, which supplies blood to the liver tumour.

Figure 1:
Changes after drug-loaded microsphere transcatheter arterial chemoembolization (DEB-TACE) in patients with breast cancer rupture and haemorrhage. [7]

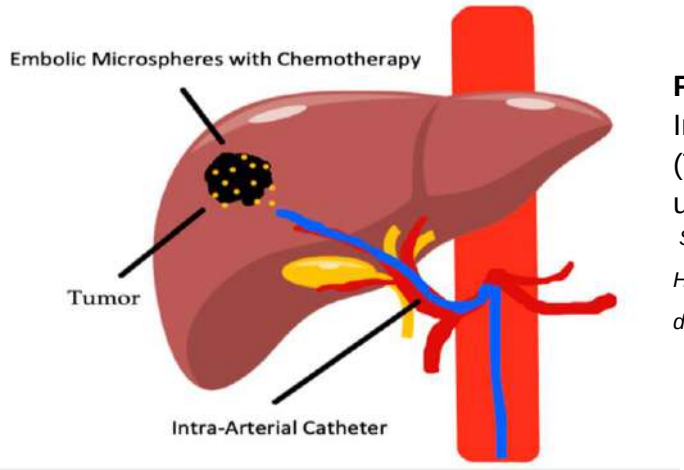

Figure 2:
Image-guided transarterial chemoembolization (TACE) of hepatic arteries supplying tumor utilizing chemotherapy drug eluting microspheres.
Santoso S,Breanna, Susman et.al.Locoregional Therapies for Hepatocellular Carcinoma in patients with nonalcoholic fatty liver disease. Biomedicine. 2024 (12) 2226

EVIDENCE SUMMARY

A total of 54 titles were retrieved from the scientific databases via OVID, PubMed and general search engines [Google Scholar], using the search term; *breast cancer, breast tumour, metastatsis*, and *chemoembolization, theraupetic.* The last search was conducted on November 2nd 2024. From the systematic search, seven studies fulfilled the inclusion and exclusion criteria. The included studies consisted of two systematic reviews (SR), one RCT, three pre and post intervention studies and one observational study.

EFFICACY/ EFFECTIVENESS

Liver Metastasis Breast Cancer (LMBC)

Aarts BM et al. (2021) conducted a systematic review and meta-analysis to evaluate the effectiveness of intra-arterial therapies, including Transarterial Chemoembolisation (TACE) and Transarterial Radioembolisation (TARE), in treating liver metastasis breast cancer (LMBC) patients. The review included studies from Netherlands, Belgium, and Spain, encompassing 26 studies with 1,266 patients, of which 10 specifically focused on TACE, involving 508 LMBC patients. One study also reported results on both TACE and TARE. The findings demonstrated that TARE and TACE showed superior effectiveness compared to chemo-infusion for treating LMBC, particularly in chemotherapy-resistant patients. TARE had the highest response rate at 49%, followed by TACE at 34%, while chemo-infusion had the lowest at 19%. Regarding overall survival (OS), TACE had the longest median survival of 17.8 months, compared to 9.2 months for TARE and 7.9 months for chemo-infusion. Subgroup analysis showed that drug-eluting beads loaded with doxorubicin (DEBDOX) TACE achieved higher response rates (46%) compared to conventional TACE (28%). The study suggests that TARE and TACE are the preferred options for LMBC patients, with chemo-infusion considered only for those not suitable for intra-arterial therapies. [9]

Wang et al. (2017) conducted a systematic review to evaluate the effectiveness and safety of Transarterial Chemoembolisation (TACE) for breast cancer with liver metastases (BCLM). This review included 10 studies with a total of 519 patients. The review reported pooled median overall survival (OS) ranging from 7.3 to 47 months and median disease-free survival (DFS) from 2.9 to 17 months. Response rates varied widely, from 7 % to 73.5%, with higher rates observed in patients with liver-only metastases. Transarterial Chemoembolisation combined with systemic chemotherapy demonstrated significantly better OS and response rates compared to systemic chemotherapy alone ($p < 0.05$).[6]

Vogl TJ et al. (2023) conducted a retrospective cohort study to evaluate the effectiveness and safety of transarterial chemoembolisation (TACE) in treating liver metastasis breast cancer (LMBC) in Germany. This study involving 549 patients treated with TACE monotherapy over 26 years. The analysis included a diverse range of patients and treatments conducted between 1993 and 2020 at Frankfurt University Hospital. The results indicated a median survival time of 0.8 years with mean time, 1.4 years has been reported for patient receiving TACE. This study also documented one, three, and five year survival rates of 37% (95% CI: 31 to 42%), 8% (95% CI: 4 to 11%), and 4% (95% CI: 2 to 7%) respectively. The findings demonstrated that TACE, while less effective than combined modalities, provides a viable option for advanced or chemo-resistant LMBC cases.[1]

Zhao GS et al. (2021) conducted an interventional study to asses the long-term clinical efficacy and safety of gelatin sponge microparticles combined with pirarubicin for hepatic transarterial chemoembolisation (GSMs-TACE) in treating liver metastases breast cancer (LMBC). A total of 27 patients underwent GSMs-TACE between July 2010 and July 2016 in China were enrolled in this study, with an average of 2.44 treatments per patient. Tumour target blood vessels were slowly and regionally embolised with absorbable gelatin sponge particles and pirarubicin injections. Plain computed tomography (CT) scans and biochemical

indexes were re-examined at four days after treatment, and enhanced CT scans or magnetic resonance images and biochemical indexes, one month later. One month after the interventional treatment, the complete respond (CR) and overall respond rate (ORR) were 25.93 and 74.07% respectively. For patients with stable tumours, the follow-up period was two to three months, and the tumour response was evaluated using Modified Response Evaluation Criteria in Solid Tumours. Results demonstrated a 96.3% disease control rate one month post-treatment, and survival rates of 62.96%, 22.22%, and 14.81% at one, three, and five years respectively, with a median overall survival of 22 months. The findings indicated that GSMs-TACE is a safe and effective localised treatment for LMBC, offering prolonged survival and manageable side effects, making it a viable option for patients unsuitable for systemic therapy or surgical resection.[10]

A pilot study by Lin et al. (2016) evaluated the effectiveness and safety of transarterial chemoembolisation (TACE) using doxorubicin-loaded drug-eluting beads for treating liver-metastatic breast cancer (LMBC) unresponsive to at least two chemotherapy regimens. This interventional study involving 23 patients was conducted from March 2012 to December 2014. During this time, all patients with progressive LMBC following the failure of two or more chemotherapy regimens were screened for participation. Results demonstrated out of 23 patients enrolled, 17 patients were completed two chemoembolization and six underwent only one session because of severe adverse events. At three months post-treatment, the disease control rate was 83%, with a median progression-free survival of eight months and overall survival of 17 months. This study highlights TACE's potential for controlling LMBC but underscores the need for strategies to mitigate its toxicities.[11]

Locally Advanced Breast Cancer (LABC)

Zhang J et al. (2024) conducted a study to investigate the effectiveness and safety of drug-eluting bead-transarterial chemoembolization (DEB-TACE) combined with systemic chemotherapy (TAC regimen) for treating hormone receptor-positive, HER2-negative (HR+/HER2-) locally advanced breast cancer (LABC) in China. This study, involving 60 LABC patients treated at Jianyang People's Hospital and the First Affiliated Hospital of Chengdu Medical College between December 2020 and June 2022. These patients were randomly assigned into two equal groups: an experimental group and a control group, each comprising 30 patients (50%). Patients in the experimental group received DEB-TACE alongside the TAC regimen (175mg/m^2 paclitaxel-loaded albumin, 50mg/m^2 cyclophosphamide), while the control group received only systemic chemotherapy. Results indicated significantly improved outcomes in the experimental group, with an Overall Response Rate (ORR) of 90% after the first treatment compared to 60% in the control group ($p < 0.05$). The total ORR reached 100% for the experimental group versus 83% for the control group ($p < 0.05$). Pathological Complete Response (PCR) was achieved in 14 patients (47%) in the experimental group and 4 patients (13%) in the control group, demonstrating higher PCR rates in the experimental group. The comparison of tumour shrinkage between the two groups showed a p-value of 0.051, while axillary lymph node shrinkage was significant at $p < 0.05$. Tumour regression was more pronounced in the experimental group particularly in the reduction of axillary lymph node metastases, with no cases of tumour progression observed.

Other Metastasis

Kennoki N et al. (2017) conducted an interventional study to evaluate the effectiveness and safety of transcatheter arterial chemoembolisation (TACE) with superabsorbent polymer microspheres (SAP-MS) for patients with pulmonary and mediastinal metastases from breast cancer in Japan. Between November 2002 and January 2015, 32 patients with pulmonary and/or mediastinal metastases from breast cancer underwent TACE. Of these, 18 were excluded for various reasons, leaving 14 female patients with a median age of 58.5 years (ranging from 37 to 77) included in the study. Transcatheter arterial chemoembolisation was repeated as needed, with indications to repeat TACE including target tumour progression and the occurrence of new tumours. The treatment demonstrated promising results, with a partial response observed in four patients (28.6%) and stable disease achieved in 10 patients (71.4%), leading to a progressive disease rate of 0%. Tumour size reduction was notable, with a median progression rate of 12.7%. Patients had a median overall survival of 29 months after the first TACE session, and a five-year survival rate of 49.5%. Multiple treatment sessions (averaging 5.5 per patient) were feasible without significant vessel damage, showcasing the treatment's adaptability for ongoing management. Despite its retrospective design and variations in drug regimens, the study concludes that TACE with superabsorbent polymer microspheres is a feasible, safe, and effective palliative treatment, providing significant local tumour control and improved survival outcomes for this patient population.[12]

SAFETY

Several studies retrieved from the scientific database that evaluated the safety profile of TACE. Some drugs used for TACE obtained approval by USFDA like Doxorubicin (oxil Liposomal/Doxorubicin Hydrochloride NDA 050718).

Two systematic reviews (SRs) found that TACE was generally associated with moderate adverse events, with grade three to four toxicities reported in 0% to 35% of cases.[9] Among these, 0% to 17.4% of patients experienced blood and liver toxicities, along with post-embolisation syndrome, including symptoms such as nausea, fever, and abdominal pain.[6]

Zhang J et al. (2024) observed adverse reactions in the experimental group after DEB-TACE, including skin blisters, pigmentation, and pain. The visual analog scale (VAS) scores ranged from three to five, with one patient requiring morphine for pain management due to VAS score greater than 7. However, no Grade III or higher adverse events were reported, and the rates of vomiting and bone marrow suppression were similar between groups.[7] Kennoki N et al. (2017) reported that the procedure was well-tolerated, with no grade three or higher haematologic toxicities. Non-haematologic toxicities included mild nausea, back pain, and fever. One patient developed grade three rash, which resolved with conservative treatment. Importantly, all procedures were completed successfully without intraoperative complications, highlighting the method's safety.[12]

Zhao GS et al. (2021) noted some post-procedure adverse events, including mild fever, abdominal pain, and nausea, all of which resolved with symptomatic management. There were no severe complications, such as liver failure or abscess.[10] In a study by Lin et al. (2016), while the procedure was technically successful in all cases, it resulted in notable

adverse events, including grade 3 toxicities like asthenia, anaemia, and liver dysfunction, which required careful management.[11]

COST/COST-EFFECTIVENESS

There was no retrievable evidence from the scientific databases on the cost/cost-effectiveness of Transarterial Chemoembolisation (TACE) for Breast Cancer. Estimated cost for TACE procedure for Breast Cancer in Germany is [redacted].[13]. The cost for this procedure in Barcelona is [redacted].[14]. Total cost per patient for the entire TACE treatment regimen in Australia is [redacted].[15] An analysis estimated total costs of this procedure in United State is approaching [redacted].[16]

CONCLUSION

The review showed that there was good level of evidence on the uses of TACE for patients with advanced breast cancer with liver metastasis. Transarterial Chemoembolisation either used alone or in combination with systemic chemotherapy improved overall survival, overall response rate and pathological complete response. There was limited evidence on locally advanced breast cancer.

REFERENCES

1. Vogl, TJ, Freichel J, Gruber-Rouh T et al. Interventional oncological treatment of breast cancer liver metastasis (BCLM): single center long-term evaluation over 26 years using thermoablation techniques like LITT, MWA and TACE in a multimodal application. International Journal of Hyperthermia, 2023 40(1)
2. Wilkinson L, Gathani T et.al.Understanding breast cancer as a global health concern. Br J Radiol. 2022 Feb 1;95(1130):20211033. doi: 10.1259/bjr.20211033. Epub 2021 Dec 14. PMID: 34905391; PMCID: PMC8822551.
3. Arnold M, Morgan E, Rumgay H et.al. Current and future burden of breast cancer: Global statistics for 2020 and 2040. The Breast. 2022 Dec 1;66:15-23.
4. Summary of Malaysia National Cancer Registry Report 2017 to 2021. Available at: https://nci.moh.gov.my/images/pdf_folder
5. Waks AG, Winer EP. Breast cancer treatment: a review. Jama. 2019 Jan 22;321(3):288-300.
6. Wang M, Zhang J, Ji S et al. Transarterial chemoembolisation for breast cancer with liver metastasis: A systematic review. The Breast. 2017 Dec 1;36:25-30.
7. Zhang J, Niu X, Zhou Y et al. Discussing the safety and effectiveness of transcatheter arterial embolization combined with intravenous chemotherapy in treating locally advanced breast cancer. Scientific Reports. 2024 Mar 12;14(1):6003.
8. West H, Jin JO et al. Transarterial Chemoembolization. JAMA Oncol. 2015;1(8):1178. doi:10.1001/jamaoncol.2015.3702
9. Aarts BM, Munoz FG, Wildiers H et al. Intra-arterial therapies for liver metastatic breast cancer: A systematic review and meta-analysis. CardioVascular and Interventional Radiology. 2021 Dec 1:1-5.
10. Zhao GS, Liu S, Liu Y et al. Clinical application of gelatin sponge microparticles combined with pirarubicin for hepatic transcatheter arterial chemoembolization in breast cancer liver metastasis treatment: results of a single-center long-term study. World Journal of Surgical Oncology. 2021 Aug 21;19(1):249.
11. Lin YT, Médioni J, Amouyal G et al. Doxorubicin-loaded 70–150 μm microspheres for liver-dominant metastatic breast cancer: results and outcomes of a pilot study. Cardiovascular and interventional radiology. 2017 Jan;40:81-9.
12. Kennoki N, Hori S, Yuki T et al. Transcatheter arterial chemoembolization with spherical embolic agent in patients with pulmonary or mediastinal metastases from breast cancer. Journal of Vascular and Interventional Radiology. 2017 Oct 1;28(10):1386-94.
13. Treatment of breast cancer with embolization or chemoembolization. Available at: https://bookinghealth.com/university-hospital-rechts-der-isar-munich/treatment-programs/689052

14. Rostambeigi N, Dekarske AS, Austin EE et.al. Cost effectiveness of radioembolization compared with conventional transarterial chemoembolization for treatment of hepatocellular carcinoma. J Vasc Interv Radiol. 2014 Jul;25(7):1075-84. doi: 10.1016/j.jvir.2014.04.014. Epub 2014 May 24. PMID: 24861664.
15. Clement W, Chenoweth A, Phipps B et al. A study comparing the cost-effectiveness of conventional and drug-eluting transarterial chemoembolisation (cTACE and DEB-TACE) for the treatment of hepatocellular carcinoma in an Australian public hospital. Journal of Medical Imaging and Radiation Oncology.10 Julai 2024.
16. Rostambeigi N, Adrienne S, Erin E et al. Cost Effectiveness of Radioembolization Compared with Conventional Transarterial Chemoembolization for Treatment of Hepatocellular Carcinoma Journal of Vascular and Interventional Radiology, Volume 25, Issue 7, 1075 - 1084

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