

臨床疫学研究室

室長 三田英治

臨床疫学研究室は主に消化器疾患の特徴を分子疫学面から検証し、最適な治療方法や安全性を検討しています。代表的な研究内容を示します。

C 型肝炎に関しては、ペグインターフェロン・リバビリン併用療法で治療効果を規定した IL-28B の SNP が引き続きインターフェロンフリー治療でも重要な意味を持つかを検討しています。また心機能低下や腎機能低下症例に対する抗 HCV 療法の安全性を調査しています。HIV 感染合併例でのインターフェロンフリー治療の成績もまとめており、抗レトロウイルス治療との薬物相互作用も検討しています。

次に B 型肝炎では、核酸アナログの長期投与成績から導かれる耐性化の問題点を検討しています。そして、ラミブジン・アデホビル併用療法効果不良例に対し、アデホビルをテノホビルに切り替えることの有効性を明らかにしました。近年散発的に発生している B 型急性肝炎では genotype A が大半を占めていますが、その特徴を解析し、慢性化への関与についても検討しています。

【2014 年度研究発表業績】

A-0

Oze T, Hiramatsu N, Yakushijin T, Miyazaki M, Iio S, Oshita M, Hagiwara H, Mita E, Inui Y, Hijioka T, Inada M, Tamura S, Yoshihara H, Inoue A, Imai Y, Miyagi T, Yoshida Y, Tatsumi T, Kanto T, Kasahara A, Hayashi N, Takehara T. Using early viral kinetics to predict antiviral outcome in response-guided pegylated interferon plus ribavirin therapy among patients with hepatitis C virus genotype 1. J Gastroenterol. 2014 Apr;49(4):737-47 (2014 年 4 月)

Harada N, Hiramatsu N, Oze T, Morishita N, Yamada R, Hikita H, Miyazaki M, Yakushijin T, Miyagi T, Yoshida Y, Tatsumi T, Kanto T, Kasahara A, Oshita M, Mita E, Hagiwara H, Inui Y, Katayama K, Tamura S, Yoshihara H, Imai Y, Inoue A, Hayashi N, Takehara T. Risk factors for hepatocellular carcinoma in hepatitis C patients with normal alanine aminotransferase treated with pegylated interferon and ribavirin. J Viral Hepat. 2014 May;21(5):357-65 (2014 年 5 月)

Oze T, Hiramatsu N, Yakushijin T, Miyazaki M, Yamada A, Oshita M, Hagiwara H, Mita E, Ito T, Fukui H, Inui Y, Hijioka T, Inada M, Katayama K, Tamura S, Yoshihara H, Inoue A, Imai Y, Hayashi E, Kato M, Miyagi T, Yoshida Y, Tatsumi T, Kasahara A, Hamasaki T, Hayashi N, Takehara T; Osaka Liver Forum. Post-treatment levels of α -fetoprotein predict incidence of hepatocellular carcinoma after interferon therapy. Clin Gastroenterol Hepatol. 2014 Jul;12(7):1186-95 (2014 年 7 月)

Hasegawa H, Fujitani K, Nakazuru S, Hirao M, Mita E, Tsujinaka T. Optimal Treatment Change Criteria for Advanced Gastric Cancer with Non-measurable Peritoneal Metastasis:symptom/tumor marker-based or CT-based. Anticancer Research 2014;34 (9):5169-5174 (2014 年 9 月)

Yajima K, Uehira T, Otera H, Koizumi Y, Watanabe D, Kodama Y, Kuzushita N, Nishida Y, Mita E, Mano M, Shirasaka T. A case of non-cirrhotic portal hypertension associated with anti-retroviral therapy in a Japanese patient with human immunodeficiency virus infection. J Infect Chemother. 2014 Sep;20(9):582-5.

Ishida H, Sakane S, Toyama T, Fukutomi K, Kimura K, Sugimoto A, Hibino K, Tamura T, Iwasaki T, Iwasaki R, Hasegawa H, Sakakibara Y, Yamada T, Nakazuru S, Mita E. Administration of low-dose epoetin-alpha facilitates adherence to ribavirin in triple therapy with pegylated interferon-alpha-2b and telaprevir. Hepatology Research 2014;44(10):E84-91 (2014 年 10 月)

Oze T, Hiramatsu N, Yakushijin T, Yamada R, Harada N, Morishita N, Oshita M, Mita E, Ito T, Inui Y, Inada M, Tamura S, Yoshihara H, Imai Y, Kato M, Miyagi T, Yoshida Y, Tatsumi T, Kasahara A, Hayashi N, Takehara T. The real impact of telaprevir dosage on the antiviral and side effects of telaprevir, pegylated interferon and ribavirin therapy for chronic hepatitis C patients with HCV genotype 1. J Viral Hepat. 2015;22(3):254-262 (2015 年 3 月)

B-2

Nakazuru S, Matsumura Y, Harada Y, Iwasaki R, Iwasaki T, Nishio K, Hasegawa H, Sakakibara Y, Yamada T, Nishikawa K, Ishida H, Mori K, Mita E. Simultaneous Large Cell Neuroendocrine Carcinoma and Adenocarcinoma of the Stomach: A Case Report and Literature Review. 12th European Neuroendocrine Tumor Society Annual Conference, Barcelona, Spain, 2015 年 3 月

Hasegawa H, Fujitani K, Sugimoto A, Nakazuru S, Hirao M, Tsujinaka T, Mita E. Optimal indications for palliative chemotherapy in elderly patients with metastatic or recurrent gastric cancer. American society of clinical oncology Gastrointestinal Cancers Symposium 2015, San Francisco, USA, 2015 年 1 月

Iwasaki T, Yamada T, Fukutomi K, Kimura K, Sugimoto A, Hibino K, Sakane S, Tamura T, Iwasaki R, Hasegawa H, Sakakibara Y, Toyama T, Nakazuru S, Ishida H, Mita E : Endoscopic submucosal dissection for elderly individuals with early gastric cancer. DDW 2014,Chicago,

USA, 2014 年 5 月

B-3

石田 永、外山 隆、三田英治：HCV/HIV 共感染者に対するペグインターフェロン/リ
バビリン併用療法の治療成績。第 50 回日本肝臓学会総会、東京、2014 年 5 月

三田英治：治療継続患者における注意点と TDF の役割。第 40 回日本肝臓学会東部会 ラ
ンチョンセミナー7、東京、2014 年 11 月

三田英治：高ストレス社会における職域肝疾患の管理 ～脂肪肝から、ウイルス性肝炎
まで～。第 22 回日本産業ストレス学会 ランチョンセミナー、大阪、2014 年 11 月

三田英治：性感染症としてのウイルス性肝炎。日本性感染症学会第 27 回学術大会 招
請講演 2、神戸、2014 年 12 月

B-4

中水流正一、福富啓祐、日比野賢嗣、杉本 彩、木村圭一、田村 猛、坂根貞嗣、岩崎
哲也、岩崎竜一郎、長谷川裕子、榊原祐子、山田拓哉、外山 隆、石田 永、池田弘
和、児玉良典、三田英治：濾胞性リンパ腫と大腸癌の同時性重複癌の 2 例。第 87 回日
本消化器内視鏡学会総会、福岡、2014 年 5 月

中水流正一、山田拓哉、浅岡忠史、宮本敦史、中森正二、三田英治：80 歳以上の高齢
者切除不能膵癌における化学療法の検討。第 45 回日本膵臓学会大会、北九州、2014
年 7 月

榊原祐子、中川健太郎、松村雄一郎、福富啓祐、杉本彩、木村圭一、日比野賢嗣、岩
崎哲也、岩崎竜一郎、西尾公美子、長谷川裕子、山田拓哉、中水流正一、石田永、三
田英治、矢嶋敬史郎、上平朝子、白阪琢磨：HIV 感染者に合併した消化管サイトメガ
ロウイルス感染症の検討。JDDW2014、神戸、2014 年 10 月

榊原祐子、福富啓祐、日比野賢嗣、杉本彩、木村圭一、坂根貞嗣、田村猛、岩崎竜一
郎、岩崎哲也、長谷川裕子、山田拓哉、中水流正一、外山隆、石田永、三田英治：当
科での難治性潰瘍性大腸炎におけるタクロリムス及びインフリキシマブによる治療成
績の検討。第 100 回日本消化器病学会総会、東京、2014 年 4 月

榊原祐子、福富啓祐、日比野賢嗣、杉本彩、木村圭一、坂根貞嗣、田村猛、岩崎竜一
郎、岩崎哲也、長谷川裕子、山田拓哉、中水流正一、外山隆、石田永、三田英治：下

部消化管内視鏡検査で指摘された HIV 感染者における尖圭コンジローマの検討。第 87 回日本消化器内視鏡学会総会、福岡、2014 年 5 月

長谷川裕子、福富啓祐、杉本彩、木村圭一、日比野賢嗣、岩崎哲也、岩崎竜一郎、榊原 祐子、山田拓哉、中水流正一、石田永、関本貢嗣、三田英治：切除不能進行大腸がんに対する一次治療としての Capecitabine+Bevacizumab 併用療法。日本消化器関連学会、神戸、2014 年 10 月

杉本 彩、中水流正一、福富啓祐、日比野賢嗣、木村圭一、田村 猛、坂根貞嗣、岩崎哲也、岩崎竜一郎、長谷川裕子、榊原祐子、山田拓哉、外山 隆、石田 永、小川吉彦、矢嶋敬史郎、上平朝子、児玉良典、三田英治：肝生検で診断された AIDS 関連バーキットリンパ腫の 2 例。第 100 回日本消化器病学会総会、東京、2014 年 4 月

杉本 彩、山田拓哉、福富啓祐、木村圭一、日比野賢嗣、坂根貞嗣、田村 猛、岩崎哲也、岩崎竜一郎、長谷川裕子、榊原祐子、外山 隆、中水流正一、石田 永、上平朝子、森 清、三田英治：HIV 感染者に発症した消化管カポジ肉腫に対する内視鏡的診断と病理組織診断との検討。第 87 回日本消化器内視鏡学会総会、福岡、2014 年 5 月

杉本 彩、中水流正一、岩崎竜一郎、長谷川裕子、榊原祐子、山田拓哉、矢嶋敬史郎、上平朝子、森 清、三田英治：化学放射線療法で完全奏効を得た HIV 感染合併肛門管扁平上皮癌の 1 例。第 12 回日本臨床腫瘍学会学術集会、福岡、2014 年 7 月

杉本 彩、長谷川裕子、福富啓祐、木村圭一、日比野賢嗣、岩崎哲也、岩崎竜一郎、榊原祐子、山田拓哉、中水流正一、石田 永、平尾素宏、三田英治：高齢者切除不能進行・再発胃癌に対する化学療法における予後因子解析。第 52 回日本癌治療学会学術集会、横浜、2014 年 8 月

杉本 彩、中水流正一、岩崎哲也、岩崎竜一郎、西尾公美子、長谷川裕子、榊原祐子、山田拓哉、石田 永、浅岡忠史、宮本敦史、中森正二、三田英治：肝内胆管癌と肝細胞癌の異時性重複癌症例の検討。第 50 回日本胆道学会学術集会、東京、2014 年 9 月

杉本 彩、山田拓哉、福富啓祐、木村圭一、日比野賢嗣、岩崎哲也、岩崎竜一郎、長谷川裕子、榊原祐子、中水流正一、石田 永、上平朝子、森 清、三田英治：HIV 感染者に発症した消化管カポジ肉腫に対する肉眼型診断と病理組織診断との検討。第 56 回日本消化器病学会大会、神戸、2014 年 10 月

日比野賢嗣、中水流正一、福富啓祐、杉本彩、木村圭一、田村猛、坂根貞嗣、岩崎哲

也、岩崎竜一郎、長谷川裕子、榊原祐子、山田拓哉、外山隆、石田永、浅岡忠史、宮本敦史、中森正二、三田英治：当院における胆道癌の重複癌の検討。第 100 回日本消化器病学会総会、東京、2014 年 4 月。

木村圭一、中水流正一、岩崎竜一郎、長谷川裕子、榊原祐子、山田拓哉、石田 永、多田雄真、森清、三田英治：胆嚢原発大細胞型神経内分泌癌の 1 例 第 12 回日本臨床腫瘍学会総会、福岡、2014 年 7 月

木村圭一、山田拓哉、榊原祐子、原口直紹、三宅正和、宮崎道彦、池田正孝、関本貢嗣、三田英治：当院における大腸 SM 癌に対する治療後経過の検討 第 69 回日本大腸肛門病学会、横浜、2014 年 11 月

三田英治：司会、セッション 15 C 型肝炎・臨床 2 第 50 回日本肝臓学会総会、東京、2014 年 5 月

三田英治：司会、一般演題（口演）20 腫瘍マーカー 第 50 回日本肝癌研究会、京都、2014 年 6 月

B-5

山田拓哉、平尾素宏、三田英治：当院における Barrett 食道癌症例の検討。日本消化器内視鏡学会近畿支部第 92 回支部例会、大阪、2014 年 6 月

榊原祐子、山田拓哉、中水流正一、三田英治：HIV 感染者に合併した消化管サイトメガロウイルス感染症の検討。第 92 回日本消化器内視鏡学会近畿支部例会、大阪、2014 年 6 月

西尾公美子、石田永、三田英治：核酸アナログ反応不良例および耐性化例に対するテノホビルの当院における治療成績、日本消化器病学会近畿支部第 102 回支部例会、京都、2015 年 2 月

岩崎竜一郎、山田拓哉、三田英治：当院における消化管粘膜下腫瘍に対する EUS-FNA の成績。日本消化器内視鏡学会近畿支部 第 92 回支部例会、大阪、2014 年 6 月

岩崎竜一郎、山田拓哉、三田英治：当院における胃腫瘍に対する内視鏡的粘膜下層剥離術(ESD)の偶発症の検討、本消化器内視鏡学会近畿支部 第 92 回支部例会、大阪、2014 年 11 月

岩崎竜一郎、山田拓哉、福富啓祐、杉本彩、木村圭一、日比野賢嗣、田村猛、坂根貞嗣、岩崎哲也、長谷川裕子、榊原祐子、中水流正一、外山隆、石田永、三田英治：
Verification of endoscopic submucosal dissection for early gastric cancer with HIV infection
(HIV 感染者における早期胃がん ESD の検討)。第 87 回 日本消化器内視鏡学会総
会、福岡、2014 年 5 月

木村圭一、榊原祐子、中川健太郎、松村雄一郎、福富啓祐、杉本彩、日比野賢嗣、
岩崎哲也、岩崎竜一郎、西尾公美子、長谷川裕子、山田拓哉、中水流正一、石田永、
三田英治：十二指腸癌を合併したクローン病の 1 例。第 93 回日本消化器内視鏡学会近
畿支部第支部例会、大阪、2014 年 11 月

清田良介、日比野賢嗣、長谷川裕子、西尾久美子、榊原祐子、山田拓哉、中水流正
一、石田永、白阪琢磨、三田英治：化学放射線療法により完全寛解が得られた HIV 感
染合併進行食道癌の 1 例。第 205 回日本内科学会近畿地方会、大阪、2014 年 9 月。

野添亜希子、西尾公美子、長谷川裕子、榊原祐子、山田拓哉、中水流正一、石田永、
三田英治、児玉良典、川端浩：瀉血の効果を経時的に肝組織で検討できたヘモクロマ
トーシスの 1 例。第 205 回日本内科学会近畿地方会、大阪、2014 年 9 月。

B-8

三田英治：CROI、EASL レポート前編。肝臓専門医育成プロジェクト 平成 26 年度 第
1 回勉強会、大阪、2014 年 4 月

三田英治：B 型肝炎 最新の話。第 13 回吹田消化器カンファレンス、吹田、2014 年
5 月

三田英治：最新の肝炎治療。赤垣クリニック治験審査委員会 100 回記念講演、大阪、2014
年 6 月

三田英治：消化器のがんにならないためにできること。日本消化器病学会近畿支部 第
51 回市民公開講座、吹田、2014 年 5 月

三田英治：B 型肝炎の最新治療。HBV infection Forum in Mie、津、2014 年 6 月

三田英治：HIV とウイルス性肝炎—治療の最前線—。Japan HIV and Hepatitis Study Group
(JHSG) 講演会、東京、2014 年 6 月

三田英治：司会、肝臓治療の今後を考える。大阪、2014 年 6 月

三田英治：司会、肝臓専門医育成プロジェクト 平成 26 年度第 2 回勉強会、大阪、2014 年 7 月

三田英治：B 型肝炎と核酸アナログ治療。定期情報誌「Expert Opinion on Hepatitis B」18 号掲載座談会、東京、2014 年 7 月

三田英治：C 型肝炎の新規治療。大阪市中心区南医師会学術講演会、大阪心斎橋、2014 年 9 月

三田英治：C 型肝炎の新規治療。中央区東・南薬剤師研修会、大阪、2014 年 10 月

三田英治：最新の C 型肝炎診療。大阪市肝炎連携講演会、大阪、2014 年 10 月

三田英治：C 型肝炎の新規治療。北区薬剤師会生涯研修会、大阪、2014 年 10 月

三田英治：B 型・C 型肝炎の新規治療。肝疾患地域連携会、大阪、2014 年 11 月

三田英治：HCV NS3 および NS5A 変異に関する検討。肝臓専門医育成プロジェクト 平成 26 年度第 3 回勉強会、大阪、2014 年 12 月

三田英治：C 型肝炎の新規治療。大阪市中心区東医師会学術講習会、大阪、2015 年 3 月

B-9

三田英治：B 型肝炎の最新治療～適正使用の観点より～。B 型肝炎 Live Meeting、大阪、2014 年 11 月

三田英治：GSK B 型慢性肝疾患治療 Webinar、株式会社フルフィルパングスタジオ大阪、2015 年 2 月

三田英治：肝臓の病気 進化する肝炎の最新治療 おはよう！ドクター#17、読売テレビ、2014 年 8 月

三田英治：肝がん 新しい検査から最新治療まで おはよう！ドクター#18、読売テレビ、2014 年 8 月

研究課題名

平成 22-24 年度国立病院機構共同臨床研究による EBM 推進のための大規模臨床研究事業：
2 型糖尿病を併せ持つ高血圧患者におけるメトホルミンの心肥大・心機能に対する効果の
検討

目的

2 型糖尿病を併せ持つ高血圧患者を対象とし、メトホルミンを投与した際の心肥大・心機能に対する効果を、心臓超音波検査による左室重量・拡張能、血中心不全バイオマーカーを指標として検討する

研究デザイン：医師主導型多施設共同非盲検ランダム化群間並行比較試験

方法：2 型糖尿病を併せ持つ高血圧患者にメトグルコを投与する群（220 名）と非投与群（220 名）。前・6 か月・12 か月後の心臓超音波検査と血中心不全バイオマーカーを測定。

結果

症例登録中。10 例の登録を行い 10 例終了。

Assertive case management versus enhanced usual care for people with mental health problems who had attempted suicide and were admitted to hospital emergency departments in Japan (ACTION-J): a multicentre, randomised controlled trial

Chiaki Kawanishi, Tohru Aruga, Naoki Ishizuka, Naohiro Yonemoto, Kotaro Otsuka, Yoshito Kamijo, Yoshiro Okubo, Katsumi Ikeshita, Akio Sakai, Hitoshi Miyaoka, Yoshie Hitomi, Akihiro Iwakuma, Toshihiko Kinoshita, Jotaro Akiyoshi, Naoshi Horikawa, Hideto Hirotsune, Nobuaki Eto, Nakao Iwata, Mototsugu Kohno, Akira Iwanami, Masaru Mimura, Takashi Asada, Yoshio Hirayasu, for the ACTION-J Group*

Summary

Background Non-fatal suicide attempt is the most important risk factor for later suicide. Emergency department visits for attempted suicide are increasingly recognised as opportunities for intervention. However, no strong evidence exists that any intervention is effective at preventing repeated suicide attempts. We aimed to investigate whether assertive case management can reduce repetition of suicide attempts in people with mental health problems who had attempted suicide and were admitted to emergency departments.

Methods In this multicentre, randomised controlled trial in 17 hospital emergency departments in Japan, we randomly assigned people aged 20 years and older with mental health problems who had attempted suicide to receive either assertive case management (based on psychiatric diagnoses, social risks, and needs of the patients) or enhanced usual care (control), using an internet-based randomisation system. Interventions were provided until the end of the follow-up period (ie, at least 18 months and up to 5 years). Outcome assessors were masked to group allocation, but patients and case managers who provided the interventions were not. The primary outcome was the incidence of first recurrent suicidal behaviour (attempted suicide or completed suicide); secondary outcomes included completed suicide and all-cause mortality. This study is registered at ClinicalTrials.gov (NCT00736918) and UMIN-CTR (C000000444).

Findings Between July 1, 2006, and Dec 31, 2009, 914 eligible participants were randomly assigned, 460 to the assertive case management group and 456 to the enhanced usual care group. We noted no significant difference in incidence of first recurrent suicidal behaviour between the assertive case management group and the enhanced usual care group over the full study period (log-rank $p=0.258$). Because the proportional hazards assumption did not hold, we did ad-hoc analyses for cumulative incidence of the primary outcome at months 1, 3, 6, 12, and 18 after randomisation, adjusting for multiplicity with the Bonferroni method. Assertive case management significantly reduced the incidence of first recurrent suicidal behaviour up to the 6-month timepoint (6-month risk ratio 0.50, 95% CI 0.32–0.80; $p=0.003$), but not at the later timepoints. Prespecified subgroup analyses showed that the intervention had a greater effect in women (up to 18 months), and in participants younger than 40 years and those with a history of previous suicide attempts (up to 6 months). We did not identify any differences between the intervention and control groups for completed suicide (27 [6%] of 460 vs 30 [7%] of 454, log-rank $p=0.660$) or all-cause mortality (46 [10%] of 460 vs 42 [9%] of 454, log-rank $p=0.698$).

Interpretation Our results suggest that assertive case management is feasible in real-world clinical settings. Although it was not effective at reducing the incidence of repetition of suicide attempts in the long term, the results of our ad-hoc analyses suggested that it was effective for up to 6 months. This finding should be investigated in future research.

Funding The Ministry of Health, Labour, and Welfare of Japan.

Introduction

Non-fatal suicide attempt is the most potent predictor of later suicide.^{1–3} Hospital admissions because of attempted suicide and self-inflicted injury have been increasing worldwide.^{3,4} The average number of admissions to emergency departments for attempted suicide and self-inflicted injury per year in the USA more than doubled from about 244 000 in 1993–96 to

538 000 in 2005–08.⁵ In the UK, roughly 220 000 patients are admitted to hospital for self-harming annually.³ Emergency department admission for attempted suicide is therefore increasingly recognised as an opportunity for medical personnel to intervene to prevent future suicide attempts.⁶

Several randomised controlled trials have been done to assess the effectiveness of contact interventions (letters or

Lancet Psychiatry 2014;
1: 193–201

See Comment page 165

*Members listed in appendix

Health Management and Promotion Center (C Kawanishi MD) and Department of Psychiatry (Y Hirayasu MD), Yokohama City University Graduate School of Medicine, Yokohama, Japan; Department of Emergency and Critical Care Medicine (T Aruga MD) and Department of Psychiatry (A Iwanami MD), Showa University School of Medicine, Tokyo, Japan; Center for Clinical Sciences, National Center for Global Health and Medicine, Tokyo, Japan (N Ishizuka PhD); Translational Medical Center, National Center of Neurology and Psychiatry, Tokyo, Japan (N Yonemoto MPH); Department of Neuropsychiatry, Iwate Medical University, Morioka, Japan (K Otsuka MD, A Sakai MD); Department of Emergency and Critical Care Medicine (Y Kamijo MD) and Department of Psychiatry (H Miyaoka MD), Kitasato University School of Medicine, Sagami, Japan; Department of Neuropsychiatry, Nippon Medical School, Tokyo, Japan (Y Okubo MD); Department of Psychiatry, Nara Medical University, Kashihara, Japan (K Ikeshita MD); Department of Neuropsychiatry, Kinki University Faculty of Medicine, Osakayama, Japan (Y Hitomi MD); Department of Psychiatry, Mito Medical Center, Mito, Japan (A Iwakuma MD); Department of Neuropsychiatry, Kansai Medical University, Hirakata, Japan (T Kinoshita MD);

Department of
Neuropsychiatry,
Oita University Faculty of
Medicine, Yufu, Japan
(J Akiyoshi MD); Department of
Psychiatry, Saitama Medical
Center, Saitama Medical
University, Kawagoe, Japan
(N Horikawa MD); Department
of Psychiatry, Osaka National
Hospital, Osaka, Japan
(H Hirotsune MD); Department
of Psychiatry, Fukuoka
University Faculty of Medicine,
Fukuoka, Japan (N Eto MD);
Department of Psychiatry,
Fujita Health University School
of Medicine, Toyoake, Japan
(N Iwata MD); Department of
Emergency Medicine,
Tsukuba Medical Center
Hospital, Tsukuba, Japan
(M Kohno MD); Department of
Neuropsychiatry,
Keio University School of
Medicine, Tokyo, Japan
(M Mimura MD); and
Department of Psychiatry,
University of Tsukuba Graduate
School of Comprehensive
Human Sciences, Tsukuba,
Japan (T Asada MD)

Correspondence to:
Dr Chiaki Kawanishi, Health
Management and Promotion
Center, Yokohama City University
Graduate School of Medicine,
22-2 Seto, Kanazawa-ku,
Yokohama, Japan
chiaki.kawanishi@gmail.com

See Online for appendix

postcards, telephone calls, home visits, etc) to prevent repetition of suicide attempts.⁷⁻¹⁷ However, no strong evidence has been produced for the effectiveness of this type of intervention.¹⁸ In their systematic review,¹⁹ O'Connor and colleagues showed that psychotherapy reduced suicide attempts in some high-risk adults in populations and settings relevant to primary care. In a randomised controlled trial,¹² cognitive therapy was effective at preventing suicide attempts in adults who had recently attempted suicide. However, the evidence overall is unclear, and the extent to which such findings are applicable to suicidal patients who are admitted to emergency departments is unknown.

Although most suicidal patients who are admitted to emergency departments are suffering from mental health problems, these patients often do not receive adequate mental health-care management in their communities after discharge.^{20,21} In a randomised controlled trial, Morthorst and colleagues²² examined the effects of assertive and intensive case management on repetition of suicide attempts, but the intervention did not lead to a significant reduction in this outcome; however, the study had a small sample size, patients were from a single centre, and individuals with psychosis were excluded from the study.

In this study, we aimed to investigate whether assertive and continuous case management could reduce the incidence of repetition of suicide attempts in adults with mental health problems who had attempted suicide, compared with enhanced usual care.

Methods

Study design and participants

ACTION-J was a multicentre, randomised controlled trial done at 17 Japanese hospitals (appendix) with both an emergency department and a psychiatric department. Potential study participants were adults (aged 20 years and older) who had attempted suicide and were admitted to the emergency department to receive critical care. To be eligible, patients had to have a primary diagnosis of an axis 1 psychiatric disorder, because the case management intervention was developed for patients with these disorders. Psychiatric diagnosis was obtained by structured interview with the Mini-International Neuropsychiatric Interview,²³ and defined as axis 1 in accordance with the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision* (DSM-IV-TR).²⁴ We excluded patients who had a primary diagnosis that did not meet the definition of a DSM-IV-TR axis 1 disorder.

Action in anticipation of death was confirmed at least twice in each patient by use of the Suicide Intent Scale.²⁵ Patients had to be able to understand the description of the study, provide informed consent, attend a face-to-face interview and a session for psychoeducation during their stay at the emergency department before enrolment in the study, and visit the participating hospital regularly to attend face-to-face

interviews for assessments and case management after discharge from the emergency department.

The study protocol was approved by the Central Research Ethics Committee of the study sponsor (Japan Foundation for Neuroscience and Mental Health, Tokyo, Japan) and by the local ethics committees of all participating hospitals. All participants provided written informed consent.

Randomisation and masking

Participants were randomly assigned (1:1) by an internet-based system operated by a central, independent data centre to either the intervention group (assertive case management) or the control group (enhanced usual care). Assignment was by the minimisation method, with four factors: participating hospital, sex, age (younger than 40 years vs 40 years and older), and history of previous suicide attempts before the current episode. We regarded these as factors that could affect the study outcomes.

Outcome assessors were masked to group assignment, but patients and case managers who provided the interventions were not. The outcome assessors, who were trained for the assessments before the trial, collected the information about attempted suicide from participants or their family members by direct interview. The assessors did not know the participants' assigned groups, the status of implementation of the intervention, or information about events obtained by other on-site staff. An event review committee independently assessed all events related to the study outcomes.

Procedures

After patients were physically stabilised and alert consciousness was confirmed, potential study participants received thorough psychosocial assessment, including assessment of the social, psychological, and motivational factors specific to the self-harm event and an assessment of mental health, social risks, and needs, as recommended by UK national clinical practice guidelines.²⁶ Trained psychiatrists in the study group checked the patients against the inclusion and exclusion criteria, and provided a complete description of the study. Next, psychiatrists or other trained medical personnel from the study group gave the patients semi-structured psychoeducation, as suggested by WHO.²⁷ After the psychoeducation session, patients were provided with the complete study description again before being asked to provide informed consent. Assigned interventions were provided until the end of the follow-up period (ie, at least 18 months and up to 5 years).

Participants who were randomly assigned to the control group received enhanced usual care at the participating emergency departments.²⁸ In addition to the psychoeducation session in the emergency department before randomisation, these participants were given an information pamphlet listing available social resources (health care-based and local government services) every time they visited for periodic assessments (6 months and

18 months after randomisation, then annually until the end of the study).

Participants who were randomly assigned to the intervention group were offered assertive and continuous case management (panel 1), delivered by dedicated case managers who were trained experts in mental health (psychiatrists, nurses, social workers, or clinical psychologists). Encouragement to participate in psychiatric treatment was a core feature and appointments with psychiatrists and primary care physicians were organised. To facilitate the case management, the psychoeducation was also provided to participants' family members during the participants' initial stay in the hospital.

The case management was provided in accordance with a manual developed by the intervention programme committee of the study group. Briefly, the case managers periodically contacted participants assigned to the intervention group for 18 months after randomisation (at week 1 and at months 1, 2, 3, 6, 12, and 18) during their stay at the emergency department and after discharge. When applicable, the case managers contacted the participants every 6 months until the end of the trial (June 30, 2011). In principle, case management was accomplished through direct dialogue (face-to-face interviews by the case managers at the hospital), or by telephone conversation as the next best option. When case managers could not reach participants, they approached family members who had given their consent in advance to be contacted; the frequency with which this approach was used was not monitored. To maintain the quality of the standardised intervention, the intervention programme committee (which consisted of the case managers and a group of the study investigators) held case conference meetings every 2 months (fidelity scores were not calculated). The

committee also visited the participating hospitals when necessary.

The protocol specified two interim analyses to assess the primary outcome, the first at roughly two-thirds into enrolment, and the second at the end of enrolment.²⁸ An independent data monitoring committee reviewed safety and efficacy issues from the interim analyses and from periodic monitoring reports

Panel 1: Features of the assertive case management intervention

- Periodic contact (either face-to-face or by telephone) with participants during their stay in the emergency department and after discharge
- Collection of information about each participant's treatment status and social problems that could disturb their treatment adherence
- Encouragement of participants to adhere to psychiatric treatment
- Coordination of appointments with psychiatrists and primary care physicians
- Encouragement of participants who discontinued psychiatric treatment to return to treatment
- Referrals to social services and private support organisations, and coordination for use of these resources to accommodate the individual needs of patients
- Provision of the psychoeducation content and information about social resources through a dedicated website

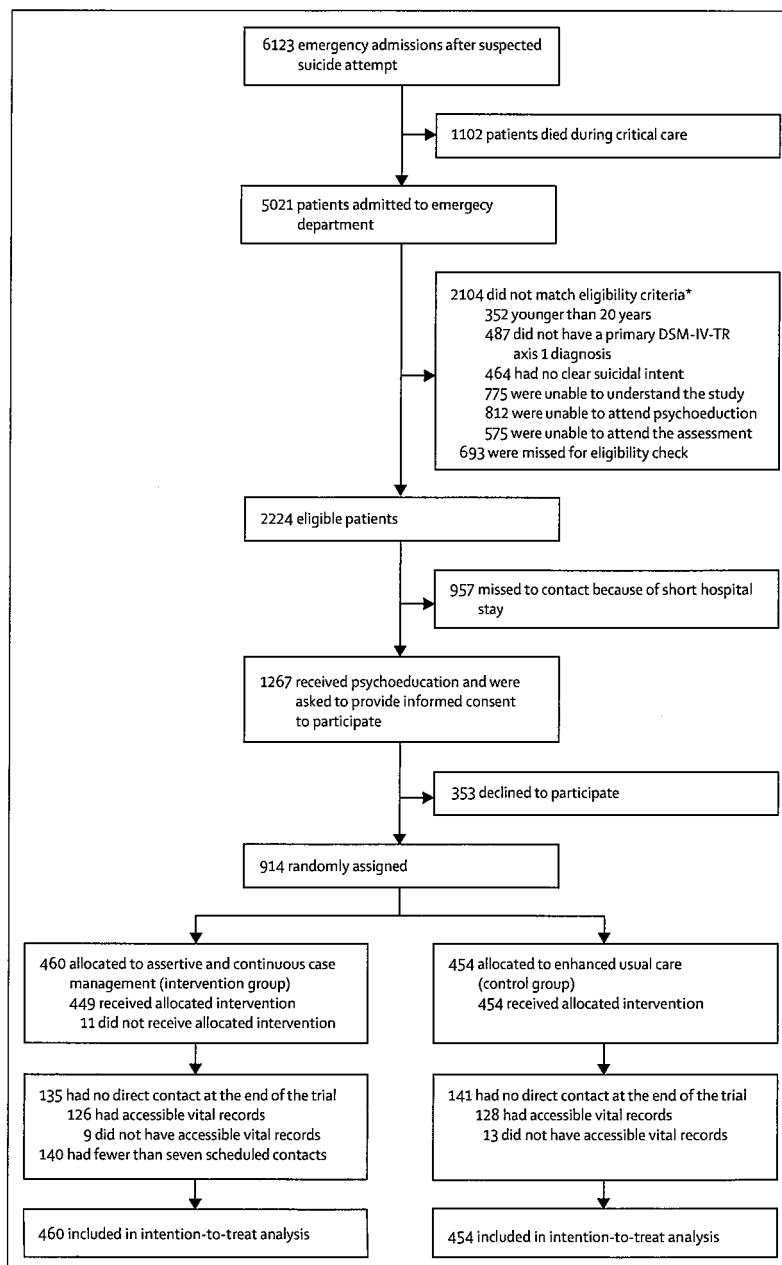


Figure 1: Trial profile

DSM-IV-TR=Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision.²⁴ *Some participants were excluded for more than one reason.

	Assertive case management group (n=460)	Enhanced usual care group (n=454)
Women	263 (57%)	251 (55%)
Mean age (years)	42.9 (14.6)	41.7 (15.2)
Older than 65 years	42 (9%)	44 (10%)
Primary psychiatric diagnosis		
Substance-related disorder	19 (4%)	26 (6%)
Schizophrenia or other psychotic disorder	93 (20%)	86 (19%)
Mood disorder	215 (47%)	211 (46%)
Adjustment disorder	100 (22%)	91 (20%)
Other	33 (7%)	40 (9%)
Visited a psychiatrist within 1 month before the suicide attempt	260 (57%)*	257 (57%)
Visited a physician other than a psychiatrist within 1 month before the suicide attempt	151 (33%)†	135 (30%)
Education		
Less than high school	115 (25%)	108 (24%)
High school	229 (50%)	237 (52%)
Beyond high school	116 (25%)	109 (24%)
Employment status		
Employed	194 (42%)	206 (45%)
Unemployed	243 (53%)	220 (48%)
Retired	11 (2%)	16 (4%)
Student	11 (2%)	12 (3%)
Missing data	1 (<1%)	0
Marital status		
Married	180 (39%)	195 (43%)
Single	169 (37%)	183 (40%)
Divorced	94 (20%)	61 (13%)
Widowed	17 (4%)	15 (3%)
Lives with partner or family	113 (25%)	84 (19%)
Previous suicide attempts		
None	229 (50%)	235 (52%)
One or two times	131 (28%)	125 (28%)
Three or more times	100 (22%)	94 (21%)
Method of the present suicide attempt‡		
Drug overdose	326 (71%)	322 (71%)
Gas	31 (7%)	28 (6%)
Laceration	76 (17%)	71 (16%)
Jumping from a high place	10 (2%)	7 (2%)
Intentional traffic-related injury	55 (12%)	60 (13%)
Hanging	27 (6%)	26 (6%)
Other	21 (5%)	21 (5%)

Data are n (%) or mean (SD). *One individual with missing data excluded from percentage calculation. †Three individuals with missing data excluded from percentage calculation. ‡Totals are greater than 100% because some individuals used more than one method.

Table 1: Baseline characteristics

produced every 3 months throughout the study period (under masking).

Outcomes

The primary outcome measure was the incidence of first recurrent suicidal behaviour (attempted suicide or

completed suicide). We also measured incidence of completed suicide and all-cause mortality as secondary outcomes to support the primary outcome measure. Because our data for the primary outcome presented time-dependent effects (the proportional hazard assumption did not hold), we also measured the cumulative incidence of the first episode of recurrent suicidal behaviour at 1, 3, 6, 12, and 18 months after randomisation as ad-hoc analyses. Information about participant deaths was obtained by the outcome assessors or from the Government death registry.

Other protocol-specified secondary outcomes were number and incidence of recurrent suicidal behaviours, including repeated suicidal attempts per person-year; number of self-harm behaviours; types and numbers of people or organisations to consult; other medical services (clinical visit or hospital admission); physical function; Beck Hopelessness Scale score;²⁹ and Health Survey for quality-of-life score (short form-36).³⁰ We plan to publish results for all these outcomes in a separate report.

Statistical analysis

We estimated that the annual incidence of first recurrent suicidal behaviour would be 15% in the control group²⁸ and 10.5% in the intervention group. Based on these estimates, we calculated that the minimum number of participants needed per group to confirm the superiority of the assertive case management intervention (with an α of 0.05 and a statistical power of 90%) was 421. In anticipation of withdrawals and missing data, we aimed to recruit 910 participants to the study.

Analyses were done in accordance with the intention-to-treat principle. To check the assumption of proportional hazards for the primary outcome, we generated an overall cumulative incidence curve using the Kaplan-Meier method and log-plot. Because our data presented time-dependent effects (the proportional hazards assumption did not hold), the hazard ratio in the survival analysis was not appropriate as a measure of effects.³¹ Therefore, we calculated risk ratios (RRs) with 95% CIs for cumulative incidence at five timepoints as ad-hoc analyses; for comparison with the results obtained from previous reports,³² we selected months 1, 3, 6, 12, and 18 after randomisation. We set α at 0.008 for adjustment of multiplicity by the Bonferroni method.³¹

We did regression analyses for the calculated RRs.³³ We also made adjustments by using regression models with the randomisation factors: sex (male vs female), age (younger than 40 years vs 40 years and older), and history of previous suicide attempts before the current episode (yes vs no). In sensitivity analyses, we did multiple imputations for missing data (at the ad-hoc timepoints) and used regression models to adjust for the randomisation factors.³⁴

We did prespecified subgroup analyses of the primary outcome (using the ad-hoc analyses for the five specified timepoints) by sex (male vs female), age (younger than 40 years vs 40 years and older), and history of previous suicide attempts before the current episode (yes vs no).

Because of the exploratory nature of the subgroup analyses, we did not make any adjustment for multiplicity. We also did a post-hoc regression analysis in each subgroup analysis to investigate the effect of the remaining randomisation factors (sex, age, and previous suicide attempts) on the primary outcome (by timepoints).

This study is registered at ClinicalTrials.gov (NCT00736918) and UMIN-CTR (C000000444).

Role of the funding source

Neither the funder nor the sponsor of the study had any role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

Of 6123 emergency admissions after suspected suicide attempt at participating hospitals between July 1, 2006, to Dec 31, 2009, 914 participants were enrolled in the study, of which 460 were randomly assigned to the intervention group (assertive case management) and 545 to the control group (enhanced usual care; figure 1). Baseline characteristics were well balanced between the groups (table 1). As planned in the protocol, two interim analyses were done during the study period (October, 2007, and June, 2008). The results of these analyses were reviewed by the independent data monitoring committee, but conclusive findings were not obtained (data not shown) and the trial was continued until the end of the study period.

The assertive case management group had fairly good adherence to the intervention at the end of the trial (figure 1); 320 (70%) of 460 participants were contacted at least seven times by a case manager. 11 (1%) participants in the assertive case management group did not receive the intervention.

With respect to the primary outcome of incidence of first recurrent suicidal behaviour, there was no difference between the two groups at the end of the study; the survival curve for the assertive case management group was not significantly different from that for the control group (log-rank $p=0.258$, Wilcoxon $p=0.103$; figure 2). However, in the ad-hoc analyses at selected timepoints (done because the proportional hazards assumption was not met), the cumulative incidence of first recurrent suicidal behaviour was significantly lower in the intervention group than in the control group at 1, 3, and 6 months after randomisation, but not at 12 or 18 months (table 2).

With respect to the secondary outcomes assessed in support of the primary outcome, we did not identify any differences between the intervention and control groups for completed suicide (27 [6%] of 460 vs 30 [7%] of 454, log-rank $p=0.660$) or all-cause mortality (46 [10%] of 460 vs 42 [9%] of 454, log-rank $p=0.698$).

In the subgroup analyses, the intervention group had a significantly lower cumulative incidence of first recurrent

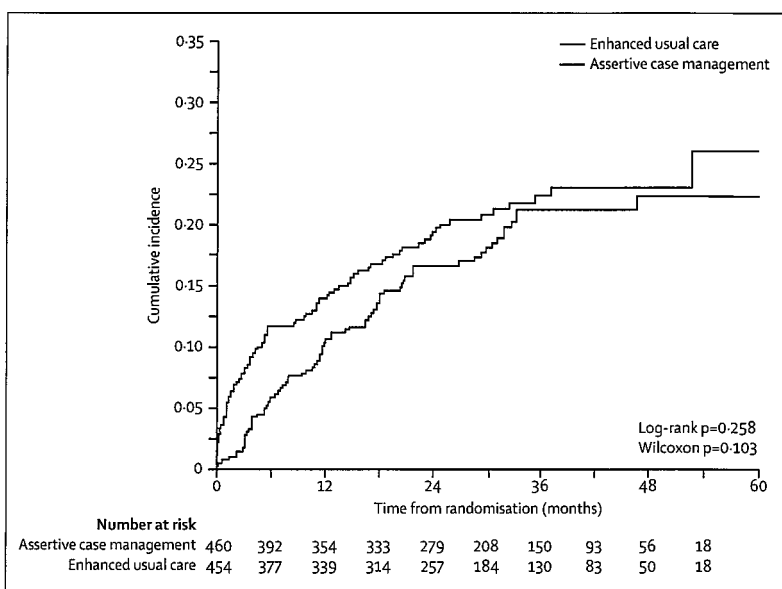


Figure 2: Kaplan-Meier curve for incidence of first episode of recurrent suicidal behaviour (attempted suicide or completed suicide)

suicidal behaviour in women (up to 18 months), and in participants younger than 40 years (up to 6 months), and those with a history of previous suicide attempts (up to 6 months). We noted no significant effect of the intervention in the other subgroups, apart from participants with no history of previous suicide attempts at 6 months only (table 3).

In the sensitivity analysis for the primary analysis, which we did to investigate possible selection bias caused by missing data, we did not find any differences from the results obtained from the primary analysis when adjusted with randomisation factors (sex, age, and previous suicide attempts; table 2), nor from the results obtained from the subgroup analyses (table 3). The sensitivity analysis in the subgroup analysis, which we did to investigate possible selection bias caused by missing data, likewise showed no differences when adjusted for remaining randomisation factors (sex, age, and previous suicide attempts; table 3).

Discussion

Our results show that assertive and continuous case management based on psychiatric diagnoses, social risks, and needs of adults who had attempted suicide was not effective at reducing the risk of repetition of suicide attempt over the full study period (follow-up time from 18 months to 5 years dependent on time of entry to the study), but it did seem to be effective for up to 6 months in our ad-hoc analyses by time from randomisation (panel 2).

Our findings are partly consistent with the results of Morthorst and colleagues' randomised controlled trial in a single Danish hospital.²² They implemented case management through assertive outreach with eight to 20 outreach consultations over 6 months by specialist nurses to

	1 month	3 months	6 months	12 months	18 months
Intervention vs control	3/444 (1%) vs 16/445 (4%)	7/430 (2%) vs 32/440 (7%)	25/417 (6%) vs 51/428 (12%)	43/397 (11%) vs 60/399 (15%)	55/380 (14%) vs 71/385 (18%)
Unadjusted risk ratio	0.19 (0.06–0.64)	0.22 (0.10–0.50)	0.50 (0.32–0.80)	0.72 (0.50–1.04)	0.79 (0.57–1.08)
Risk ratio (imputed)*	0.19 (0.05–0.63)	0.22 (0.10–0.48)	0.48 (0.31–0.77)	0.71 (0.49–1.02)	0.77 (0.55–1.06)
Risk ratio (adjusted)†	0.19 (0.05–0.60)	0.22 (0.10–0.49)	0.49 (0.31–0.77)	0.72 (0.50–1.04)	0.78 (0.57–1.07)
Risk ratio (imputed plus adjusted)‡	0.18 (0.05–0.60)	0.21 (0.09–0.47)	0.47 (0.30–0.75)	0.70 (0.48–1.00)	0.75 (0.54–1.03)

Data are number of events/population for the intervention (assertive case management) group or control (enhanced usual care) group, or risk ratio (95% CI). *Risk ratios with data imputed for individuals who missed the assessment. †Risk ratios adjusted by use of regression models for the randomisation factors of sex, age, and history of previous suicide attempts before the current episode. ‡Risk ratios with data imputed for individuals who missed the assessment and adjusted by use of regression models for the randomisation factors of sex, age, and history of previous suicide attempts before the current episode.

Table 2: First recurrent suicidal behaviour (attempted suicide or completed suicide), by timepoint (ad-hoc analysis)

improve adherence with after-treatment as an add-on to standard treatment. The intervention did not show a significant reduction of repetition of suicide attempt at 12 months (OR 0.69, 95%CI 0.34–1.43).

In our trial, adherence to the intervention was 70% (figure 1). After 6 months, the case management was provided every 6 months until the end of the follow-up period (ie, from 18 months to 5 years after randomisation), whereas before 6 months it was provided more often. The less frequent intervention after 6 months might have weakened the effectiveness of the intervention, although intervention might be effective only for a short period of time. Our results suggest that continuous case management needs to be taken over by community mental health caregivers within 6–12 months, dependent on the availability of medical and social resources in the community.

Because of the high adherence to our intervention programme and the fact that the trial design was embedded in real-world clinical settings, our study shows that the assertive case management intervention is feasible in clinical practice, with social workers or medical personnel playing the part of case managers. Our findings could also be relevant outside of Japan, in other countries with functioning emergency services and comprehensive mental health care services in place.

The subgroup analyses showed that greater effects were seen in women, participants younger than 40 years, and those with a history of previous suicide attempts. Patients attempting suicide constitute a heterogeneous group, differing in age, livelihood conditions, and risk factors. Further research is needed to examine why a greater effect was seen in these specific subgroups.

We noted no difference in the incidence of completed suicide between groups during the overall study period. In their randomised trial, Fleischmann and colleagues¹⁵ reported significantly fewer deaths by suicide among people who had attempted suicide who were given brief intervention and contact than among those given treatment as usual at the 18-month follow-up. However, their trial was deliberately done in five low-resource countries with little infrastructure and scarce financial and human resources. They noted that treatment as usual for the participating sites in their study “would

not cover routine or systematic psychiatric or psychological assessment or help”, whereas in Japan psychiatric consultation was available at 76% of the registered tertiary emergency medical centres in 2012,³⁵ although only some of these centres provided routine psychiatric assessment.

Our study had some limitations. First, the enhancement of usual care might have affected the overall results of our study, since the control group received better care than is usual in clinical practice in Japan. We chose to use enhanced usual care as the comparison group for ethical reasons; however, this approach might have reduced the difference in the primary outcome between the assertive case management group and the control group.

Another limitation of our study is that it did not include suicidal patients younger than 20 years. These patients were excluded because individuals younger than 20 years are regarded as minors in Japan and informed consent has to be obtained from legal guardians. Additionally, we excluded suicidal patients without an axis 1 DSM-IV-TR disorder as their primary diagnosis because the intervention was designed specifically for patients with an axis 1 disorder.

Many individuals who had attempted suicide did not participate in the study because their physical conditions were too severe for them to understand the description of the study, and to attend the interview and session for psychoeducation. Additionally, we missed some people who had attempted suicide for eligibility review or contact for the informed consent because of their short hospital stay. Our results might have some selection bias; we could not collect data for people who did not participate in our study because of ethical restrictions. However, the characteristics of our study participants were similar to those described in a national registry study.⁵

Although the outcomes were systematically collected from participants and official records, our results might have some reporting bias. Additionally, we could not compare the self-reported outcome of suicidal behaviour by participants with register data for admissions to emergency wards for critical care or hospital contacts because it was impossible to track all register data or hospital contacts since the catchment areas of some emergency services in urban areas in Japan overlap, and

	1 month	3 months	6 months	12 months	18 months
Sex					
Men (n=400)					
Intervention vs control	2/190 (1%) vs 3/202 (1%)	4/184 (2%) vs 9/200 (5%)	10/178 (6%) vs 17/197 (9%)	18/172 (10%) vs 21/183 (11%)	24/168 (14%) vs 25/177 (14%)
Unadjusted risk ratio	0.69 (0.12-4.07)	0.48 (0.15-1.54)	0.65 (0.31-1.38)	0.91 (0.50-1.65)	1.01 (0.60-1.70)
Risk ratio (imputed)*	0.79 (0.13-4.66)	0.46 (0.14-1.46)	0.61 (0.29-1.29)	0.88 (0.48-1.61)	0.99 (0.59-1.67)
Risk ratio (adjusted)†	0.79 (0.13-4.66)	0.48 (0.15-1.52)	0.64 (0.30-1.36)	0.90 (0.50-1.62)	0.99 (0.60-1.66)
Risk ratio (imputed plus adjusted)‡	0.76 (0.13-4.48)	0.45 (0.14-1.44)	0.60 (0.28-1.27)	0.87 (0.48-1.57)	0.96 (0.57-1.62)
Women (n=514)					
Intervention vs control	1/254 (<1%) vs 13/243 (5%)	3/246 (1%) vs 23/240 (10%)	15/239 (6%) vs 34/231 (15%)	25/225 (11%) vs 39/216 (18%)	31/212 (15%) vs 46/208 (22%)
Unadjusted risk ratio	0.07 (0.01-0.56)	0.13 (0.04-0.43)	0.43 (0.24-0.76)	0.62 (0.39-0.98)	0.66 (0.44-0.99)
Risk ratio (imputed)*	0.07 (0.01-0.56)	0.13 (0.04-0.41)	0.42 (0.24-0.75)	0.61 (0.38-0.98)	0.64 (0.42-0.98)
Risk ratio (adjusted)†	0.07 (0.01-0.54)	0.13 (0.04-0.41)	0.43 (0.24-0.76)	0.64 (0.40-1.00)	0.66 (0.44-0.99)
Risk ratio (imputed plus adjusted)‡	0.01 (0.04-0.55)	0.12 (0.04-0.40)	0.42 (0.24-0.74)	0.61 (0.38-0.96)	0.63 (0.42-0.95)
Age					
Younger than 40 years (n=453)					
Intervention vs control	0/216 vs 12/222 (5%)	3/210 (1%) vs 23/221 (10%)	14/204 (7%) vs 37/216 (17%)	27/193 (14%) vs 41/207 (20%)	32/186 (17%) vs 49/200 (25%)
Unadjusted risk ratio	..	0.14 (0.04-0.45)	0.40 (0.22-0.72)	0.71 (0.45-1.10)	0.70 (0.47-1.05)
Risk ratio (imputed)*	..	0.13 (0.04-0.43)	0.38 (0.21-0.69)	0.67 (0.43-1.05)	0.66 (0.44-0.99)
Risk ratio (adjusted)†	..	0.13 (0.04-0.43)	0.39 (0.22-0.69)	0.69 (0.44-1.07)	0.68 (0.46-1.01)
Risk ratio (imputed plus adjusted)‡	..	0.13 (0.04-0.42)	0.37 (0.21-0.67)	0.65 (0.41-1.01)	0.64 (0.43-0.96)
Older than 40 years (n=461)					
Intervention vs control	3/228 (1%) vs 4/223 (2%)	4/220 (2%) vs 9/219 (4%)	11/213 (5%) vs 14/212 (7%)	16/204 (8%) vs 19/192 (10%)	23/194 (12%) vs 22/185 (12%)
Unadjusted risk ratio	0.73 (0.17-3.24)	0.44 (0.14-1.41)	0.78 (0.36-1.68)	0.79 (0.42-1.50)	1.00 (0.58-1.73)
Risk ratio (imputed)*	0.72 (0.16-3.19)	0.43 (0.13-1.37)	0.76 (0.35-1.63)	0.81 (0.43-1.54)	1.01 (0.58-1.75)
Risk ratio (adjusted)†	0.81 (0.18-3.59)	0.45 (0.14-1.43)	0.80 (0.37-1.73)	0.81 (0.43-1.52)	0.99 (0.58-1.72)
Risk ratio (imputed plus adjusted)‡	0.78 (0.18-3.48)	0.43 (0.13-1.38)	0.77 (0.36-1.67)	0.82 (0.43-1.54)	1.00 (0.57-1.74)
Previous suicide attempt					
None (n=464)					
Intervention vs control	1/223 (<1%) vs 3/234 (1%)	3/216 (1%) vs 10/230 (4%)	7/207 (3%) vs 19/220 (9%)	14/202 (7%) vs 21/204 (10%)	17/192 (9%) vs 24/198 (12%)
Unadjusted risk ratio	0.35 (0.04-3.34)	0.32 (0.09-1.15)	0.39 (0.17-0.91)	0.67 (0.35-1.29)	0.73 (0.41-1.32)
Risk ratio (imputed)*	0.34 (0.04-3.27)	0.31 (0.09-1.10)	0.38 (0.16-0.88)	0.68 (0.36-1.31)	0.73 (0.40-1.32)
Risk ratio (adjusted)†	0.36 (0.04-3.40)	0.33 (0.09-1.18)	0.41 (0.18-0.95)	0.70 (0.37-1.34)	0.75 (0.42-1.34)
Risk ratio (imputed plus adjusted)‡	0.35 (0.04-3.32)	0.32 (0.09-1.13)	0.39 (0.17-0.91)	0.70 (0.37-1.34)	0.73 (0.41-1.33)
One or more (n=450)					
Intervention vs control	2/221 (1%) vs 13/211 (6%)	4/214 (2%) vs 22/210 (10%)	18/210 (9%) vs 32/208 (15%)	29/195 (15%) vs 39/195 (20%)	38/188 (20%) vs 47/187 (25%)
Unadjusted risk ratio	0.15 (0.03-0.64)	0.18 (0.06-0.51)	0.56 (0.32-0.96)	0.74 (0.48-1.15)	0.80 (0.55-1.17)
Risk ratio (imputed)*	0.15 (0.03-0.64)	0.17 (0.06-0.49)	0.53 (0.31-0.92)	0.71 (0.45-1.10)	0.77 (0.52-1.12)
Risk ratio (adjusted)†	0.14 (0.03-0.61)	0.17 (0.06-0.49)	0.53 (0.31-0.91)	0.73 (0.57-1.12)	0.78 (0.54-1.14)
Risk ratio (imputed plus adjusted)‡	0.14 (0.03-0.62)	0.17 (0.06-0.48)	0.51 (0.30-0.88)	0.69 (0.44-1.06)	0.74 (0.51-1.09)
Data are number of events/population for the intervention (assertive case management) group or control (enhanced usual care) group, or risk ratio (95% CI). *Risk ratios with data imputed for individuals who missed the assessment. †Risk ratios adjusted by use of regression models for the randomisation factors of sex, age, and history of previous suicide attempts before the current episode. ‡Risk ratios with data imputed for individuals who missed the assessment and adjusted by use of regression models for the randomisation factors of sex, age, and history of previous suicide attempts before the current episode.					

Table 3: First recurrent suicidal behaviour (attempted suicide or completed suicide), by subgroup (ad-hoc analysis by timepoint)

Panel 2: Research in context

Systematic review

We searched PubMed for articles published from Jan 1, 1949, to Feb 28, 2014, using the search terms "suicid*" OR "self-harm" OR "self-injury" AND "random*" OR "interventions". We identified 12 relevant systematic reviews of randomised trials; the most recent systematic review was by O'Connor and colleagues,¹⁹ which showed that psychotherapy reduced suicide attempts in some high-risk adults in populations and settings relevant to primary care. In a recent randomised trial, Morthorst and colleagues²² examined the effects of assertive and intensive case management on repetition of suicide attempt, but the intervention did not lead to a significant reduction in repetition of suicide attempt.

Interpretation

In our large, multicentre, randomised controlled trial assertive case management was feasible in real-world clinical settings for suicidal patients with psychiatric disorders admitted to the emergency department. Although it was not effective at reducing the incidence of repetition of suicide attempts in the long term, the results of our ad-hoc analyses suggested that it was effective for up to 6 months. Our results also suggest potentially heterogeneous effects of assertive case management; the intervention seemed to be more effective in women, participants younger than 40 years, and those with a history of previous suicide attempts.

some participants might have moved out of the catchment areas. Finally, although outcome data were collected by trained assessors, possible variability of the assessments might have introduced bias into the results.

Contributors

YHir, CK, TA, NI, and NY conceived and designed the study. YHir was the principal investigator. YHir, CK, KO, YO, KI, AS, HM, YHit, Alwak, TK, JA, NH, HH, NE, NI, MK, Alwan, MM, and TA enrolled patients. YHir, CK, KO, YK, YO, KI, AS, HM, YHit, Alwak, TK, JA, NH, HH, NE, NI, MK, Alwan, MM, and TA managed the study at the participating sites. NI and NY analysed the data. CK wrote the first draft of the report. YHir, TA, KO, YK, YO, KI, AS, HM, YHit, Alwak, TK, JA, NH, HH, NE, NI, MK, Alwan, MM, and TA contributed to the writing of the report.

Declaration of interests

We declare no competing interests.

Acknowledgments

This study was funded by the Ministry of Health, Labour, and Welfare of Japan. We thank the participating hospitals for their cooperation. We thank Mitsuhiro Yamada and Masatoshi Inagaki from the National Center of Neurology and Psychiatry (Tokyo, Japan) for their helpful assistance. We also thank Navneet Kapur from the University of Manchester (Manchester, UK) for providing comments on the report. Finally, we express our deepest sorrow for the loss of Toshiharu Fujita, who greatly contributed to the design of this trial.

References

- 1 Isometsä ET, Lönnqvist JK. Suicide attempts preceding completed suicide. *Br J Psychiatry* 1998; **173**: 531–35.
- 2 Da Cruz D, Pearson A, Saini P, et al. Emergency department contact prior to suicide in mental health patients. *Emerg Med J* 2011; **28**: 467–71.
- 3 Nordentoft M, Mortensen PB, Pedersen CB. Absolute risk of suicide after first hospital contact in mental disorder. *Arch Gen Psychiatry* 2011; **68**: 1058–64.

- 4 Hawton K, Bergen H, Casy D, et al. Self-harm in England: a tale of three cities. *Soc Psychiatry Psychiatr Epidemiol* 2007; **42**: 513–21.
- 5 Ting SA, Sullivan AF, Boudreaux ED, Miller I, Camargo CA Jr. Trends in US emergency department visits for attempted suicide and self-inflicted injury, 1993–2008. *Gen Hosp Psychiatry* 2012; **24**: 557–65.
- 6 D'Onofrio G, Jauch E, Jagoda A, et al. NIH roundtable on opportunities to advance research on neurologic and psychiatric emergencies. *Ann Emerg Med* 2010; **56**: 551–64.
- 7 Gibbons JS, Butler J, Urwin P, Gibbons JL. Evaluation of a social work service for self-poisoning patients. *Br J Psychiatry* 1978; **133**: 111–18.
- 8 Allard R, Marshall M, Plante MC. Intensive follow-up does not decrease the risk of repeat suicide attempts. *Suicide Life Threat Behav* 1992; **22**: 303–14.
- 9 van Heeringen C, Jannes S, Buylaert W, Henderick H, De Bacquer D, van Remoortel J. The management of non-compliance with referral to out-patient after-care among attempted suicide patients: a controlled intervention study. *Psychol Med* 1995; **25**: 963–70.
- 10 van der Sande R, van Rooijen L, Buskens E, et al. Intensive in-patient and community intervention versus routine care after attempted suicide. A randomised controlled intervention study. *Br J Psychiatry* 1997; **171**: 35–41.
- 11 Cedereke M, Monti K, Öjehagen A. Telephone contact with patients in the year after a suicide attempt: does it affect treatment attendance and outcome? A randomised controlled study. *Eur Psychiatry* 2002; **17**: 82–91.
- 12 Brown GK, Have TT, Henriques GR, Xie SX, Hollander JE, Beck AT. Cognitive therapy for the prevention of suicide attempts. *JAMA* 2005; **294**: 563–70.
- 13 Vaiva G, Vaiva G, Ducrocq F, et al. Effect of telephone contact on further suicide attempts in patients discharged from an emergency department: randomised controlled study. *BMJ* 2006; **332**: 1241–45.
- 14 Carter GL, Clover K, Whyte IM, Dawson AH, D'Este C. Postcards from the EDge: 24-month outcomes of a randomised controlled trial for hospital-treated self-poisoning. *Br J Psychiatry* 2007; **191**: 548–53.
- 15 Fleischmann A, Bertolote JM, Wasserman D, et al. Effectiveness of brief intervention and contact for suicide attempters: a randomized controlled trial in five countries. *Bull World Health Organ* 2008; **86**: 703–09.
- 16 Beautrais AL, Gibb SJ, Faulkner A, Fergusson DM, Mulder RT. Postcard intervention for repeat self-harm: randomised controlled trial. *Br J Psychiatry* 2010; **197**: 55–60.
- 17 Hassani-Moghaddam H, Sarjani S, Kolahi A, Carter GL. Postcards in Persia: randomised controlled trial to reduce suicidal behaviours 12 months after hospital-treated self-poisoning. *Br J Psychiatry* 2011; **198**: 309–16.
- 18 Kapur N, Cooper J, Bennet O, Gunnel D, Hawton K. Postcards, green cards and telephone calls: therapeutic contact with individuals following self-harm. *Br J Psychiatry* 2010; **197**: 5–7.
- 19 O'Connor EA, Gaynes BN, Burda BU, Soh C, Whitlock EP. Screening for and treatment of suicide risk relevant to primary care: a systematic review for the US Preventive Service Task Force. *Ann Intern Med* 2013; **158**: 741–54.
- 20 Gairin I, House A, Owens D. Attendance at the accident and emergency department in the year before suicide: retrospective study. *Br J Psychiatry* 2003; **183**: 28–33.
- 21 Olsson M, Marcus SC, Bridge JA. Emergency treatment of deliberate self-harm. *Arch Gen Psychiatry* 2012; **69**: 80–88.
- 22 Morthorst B, Krogh J, Erlangsen A, Alberdi F, Nordentoft M. Effect of assertive outreach after suicide attempt in the AID (assertive intervention for deliberate self harm) trial: randomised controlled trial. *BMJ* 2013; **345**: e4972.
- 23 Sheehan DV, Lecrubier Y, Sheehan KH, et al. The Mini-International Neuro-mental Interview (MINI): the development and validation of a structured diagnostic mental interview for DSM-IV and ICD-10. *J Clin Psychiatry* 1998; **59**: 22–33.
- 24 American Psychiatric Association. Diagnostic and statistical manual of mental disorders, fourth edition, text revision. Washington, DC: American Psychiatric Association, 2000.
- 25 Beck A, Schuyler D, Herman J. Development of suicidal intent scales. In: Beck A, Resnik H, Lettieri DJ, eds. The prediction of suicide. Bowie: Charles Press, 1975: 45–56.

- 26 National Collaborating Centre for Mental Health. Self-harm: the short-term physical and psychological management and secondary prevention of self-harm in primary and secondary care. In: National Clinical Practice Guideline Number 16. Leicester and London: British Psychological Society and Royal College of Psychiatrists, 2004.
- 27 WHO. Multisite intervention study on suicidal behaviours SUPRE-MISS: protocol of SUPREMISS. Geneva: World Health Organization, 2002.
- 28 Hirayasu Y, Kawanishi C, Yonemoto N, et al. A randomized controlled multicenter trial of post-suicide attempt case management for the prevention of further attempts in Japan (ACTION-J). *BMC Public Health* 2009; 9: 364.
- 29 Beck AT, Brown G, Berchick RJ, Stewart BL, Steer RA. Relationship between hopelessness and ultimate suicide: a replication with psychiatric outpatients. *Am J Psychiatry* 1990; 147: 190–95.
- 30 Fukuhara S, Bito S, Green J, Hsiao A, Kurokawa K. Translation, adaptation, and validation of the SF-36 Health Survey for use in Japan. *J Clin Epidemiol* 1998; 51: 913–23.
- 31 Chow S-C, Liu J-P. Design and analysis of clinical trials: concept and methodologies, 2nd edn. Hoboken: Wiley, 2004.
- 32 Hawton K, Townsend E, Arensman E, et al. Psychosocial versus pharmacological treatments for deliberate self harm. *Cochrane Database Syst Rev* 2000; 2: CD001764.
- 33 McNutt LA, Wu C, Xue X, Hafner JP. Estimating the relative risk in cohort studies and clinical trials of common outcomes. *Am J Epidemiol* 2003; 157: 940–43.
- 34 Carpenter J, Kenward M. Multiple imputation and its application. Hoboken: Wiley, 2013.
- 35 Ministry of Health, Labour, and Welfare of Japan. Survey of tertiary emergency medical centers in Japan (in Japanese). <http://www.mhlw.go.jp/stf/shingi/2r985200000335ux-att/2r9852000003361c.pdf> (accessed July 1, 2014).

厚生労働科学研究委託事業 難治性疾患実用化研究事業

「特発性大腿骨頭壊死症の治療法確立と革新的予防法開発にむけた全国学際研究」

大腿骨頭壊死症に関する薬物予防治療に関する研究、人工股関節等の外科的治療に関する研究がおこなわれており。当院の関わりとしては、当該疾患の外科的治療の成績の長期追跡調査から外科的治療の有効な選択を明らかにする目的で本事業の中におかれた人工関節治療 registry に症例を登録することで寄与している。現在 210 例の患者登録をしており、当該事業のデータの根幹となっている。

厚生労働科学研究補助金 難治性疾患等政策研究事業

「特発性大腿骨頭壊死症の疫学調査・診断基準・重症度分類の改訂と診療ガイドライン策定を目指した大規模多施設研究」

特発性大腿骨頭壊死症の疫学については過去に報告は多数あったが、バイアスのかかった一面的な解析データが主であったため、正確な統計学的手法を用い、その疫学を明らかにしようとする研究事業であり、本年度から全国疫学調査が開始となっている。当院はその対象施設となっており、今後データの供出によって本事業に貢献していく予定である。

PCPS システムにおけるキャビテーションによる 気泡発生 の検討

国立病院機構 大阪医療センター 臨床工学技士

藤井 順也

I. 緒言

経皮的心肺補助法（PCPS：Percutaneous Cardio Pulmonary Support system）は、クリティカルケア領域で心肺機能の補助として広く用いられている。PCPS では、患者から脱血した静脈血が遠心ポンプに送られ、そこから人工肺で酸素化されたのち患者の動脈へ返血される。その際、遠心ポンプ内では、プロペラが高速で回転することにより生まれる遠心力を利用して血液を送りだしているが、ひとたび脱血不良の状態におかれるとキャビテーションによる気泡発生を誘発することは広く知られている¹⁾²⁾³⁾。しかし、臨床上 PCPS 使用中の脱血不良は避けられない事象である。閉鎖型回路である PCPS において回路内に空気が混入すると、脳などの毛細血管へ直接送られ重篤な空気塞栓症を引き起こす危険性があるが、キャビテーションによる気泡は目視で確認できないほど小さいため⁴⁾⁵⁾放置されることが多く、その危険性が重要視されていない。本研究ではキャビテーションによる気泡発生 の程度、PCPS の設定条件との関連性を検討したので報告する。

II. 方法

1. 実験回路

実験回路図を図 1 に示す。実験溶液には、模

擬血液としてグリセリン（分子量 92Da,和光純薬、大阪）を Reverse Osmosis water（RO 水）に溶解し、40vol%グリセリン水溶液になるように調整した。PCPS 回路は、熱交換器付回路（テルモ EBS 回路、テルモ株式会社、東京）使用し、気泡計測器（ultrasonic Bubble Detector CMD-20, Hatteland Inc, norway）を用いて、遠心ポンプ入口側（脱血側）と人工肺出口側（送血側）にて発生する気泡を測定した。閉塞率の調整には、オクルーダー（HAS II - RE, 泉工医科工業、埼玉）を使用。送脱血カニューレは、経皮的挿入カニューレ（カニューレ（CBAS）、Medtronic Inc, 米国）脱血 23Fr、送血 15Fr、17Fr、19Fr を使用した。また、回路内には、十分な除泡を行うためリザーバーを設置した。

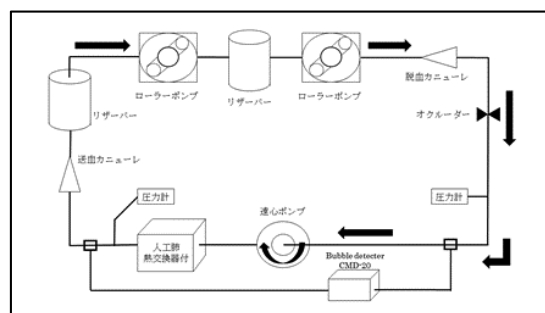


図 1 実験回路構成

2. 実験条件

実験の各種条件の組合せを図2に示す。基本条件として、人工肺に流すガス（Flow：3.0L/min、FiO₂：60%）、回路内温度を36.0℃に設定し、これを基にFlow、FiO₂、温度を1つずつ変化させた。これに遠心ポンプの回転数と回路閉塞率の各種条件を変化させた全ての組合せ375通りについて、送血管の3サイズ（15、17、19Fr）の変更を加えた975通り全てにおける気泡発生についてのデータ採取を行った。各々の詳細に付いては以下に述べる。

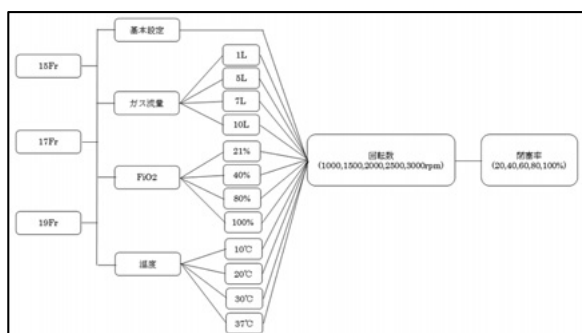


図2 実験条件フローチャート

2-1. ガス条件と温度変化

人工肺に流すガス流量を1、3、5、7、10L/minの5段階に変化をさせ、同様にFiO₂も21、40、60、80、100%の5段階に変化させた。また、回路内温度についても10、20、30、36、37℃の5段階に変化させた。ただし、1つの条件を変更する際は他の条件を基本条件に戻すこととした。

2-2. 回転数と閉塞率の変化

回転数は、1000から3000rpmまで500rpmごとの5段階に変化させ、同様に回路の閉塞率についても20～100%までの20%ごとの5段階について変化させた。気泡測定条件は、全ての組合せについて10秒間とし各々5回ずつ測定した。

III. 結果

各種条件における測定結果を表1に示す。気泡（バブル）発生については、ガス条件や温度変化に比べ回転数と閉塞率を変化させた場合に発生率が高かった。また、脱血側と送血側で

は、脱血側でより多くのバブル数を認めたため脱血側での回転数と閉塞率を基に気泡発生条件を整理し、ガス条件と温度変化について解析を行った。また、脱血側と送血側でのバブル数との関係性については、人工肺での気泡除去との関係が考えられるため別途解析を行った。詳細を以下に示す。

1. 回転数と閉塞率が気泡発生におよぼす影響

回転数とバブル数の関係を図3に示す。回転数とバブル数の関係を見ると送血管の太さに関係なく回転数の増加にともないバブルの数は正比例的に増加し、2500rpm以上では明らかなバブル発生を認める傾向が強かった。また、閉塞率別にみると閉塞率を増すごとにバブル数は増加し、その後閉塞率80%で最大を迎え閉塞率100%では収束する結果となった。しかし、バブル発生時のバブル数にはバラつきがあり、他の条件が関与することを示唆する結果となった。

2. 回転数と模擬血液流量の関係

回転数と模擬血液流量の関係性を図4に示す。回転数と流量の関係を見ると閉塞率や送血管の太さに関係なく全ての条件において回転数の増加に伴い流量の増加を認めた。また、これらの関係性について回帰分析を行ったところ高い寄与率を示し強い正の相関を示す結果となった。

3. 係数とバブル数の関係

回転数と流量の関係性において強い正の相関を認めたことから流量を回転数で除して求められたものを係数とし、係数とバブル数の関係性について図5に示した。図5における回転数については図3より明らかなバブル発生を認めた回転数2500rpm以上での関係性についてのみ示している。図5よりバブル数が多く発生する係数値は0.8～1.4（mL / rpm・min）の範囲で集中しており、回転数と流量の2つの要素を含む係数がバブル数におよぼす影響に大きく関与することが示された。また、送血側と脱血側での比較においてもバブル数での若干の差は認め

表 1 各条件における測定結果

1区：基本設定				1区：基本設定				1区：基本設定			
回遊数 (Count)	回遊率 (%)	観測回パブル数 (Count±SD)	観測回パブル数 (Count±SD)	回遊数 (Count)	回遊率 (%)	観測回パブル数 (Count±SD)	観測回パブル数 (Count±SD)	回遊数 (Count)	回遊率 (%)	観測回パブル数 (Count±SD)	観測回パブル数 (Count±SD)
1000	30	0±0	0±0	1000	30	0±0	0±0	1000	30	0±0	0±0
	40	0±0	0±0		40	0±0	0±0		40	0±0	0±0
	50	0±0	0±0		50	0±0	0±0		50	0±0	0±0
	60	0±0	0±0		60	0±0	0±0		60	0±0	0±0
	70	0±0	0±0		70	0±0	0±0		70	0±0	0±0
1800	100	0±0	0±0	1800	100	0±0	0±0	1800	100	0±0	0±0
	30	0±0	0±0		30	0±0	0±0		30	0±0	0±0
	40	0±0	0±0		40	0±0	0±0		40	0±0	0±0
	50	0±0	0±0		50	0±0	0±0		50	0±0	0±0
	60	0±0	0±0		60	0±0	0±0		60	0±0	0±0
3000	100	0±0	0±0	3000	100	0±0	0±0	3000	100	0±0	0±0
	30	0±0	0±0		30	0±0	0±0		30	0±0	0±0
	40	0±0	0±0		40	0±0	0±0		40	0±0	0±0
	50	0±0	0±0		50	0±0	0±0		50	0±0	0±0
	60	0±0	0±0		60	0±0	0±0		60	0±0	0±0
5000	100	0±0	0±0	5000	100	0±0	0±0	5000	100	0±0	0±0
	30	0±0	0±0		30	0±0	0±0		30	0±0	0±0
	40	0±0	0±0		40	0±0	0±0		40	0±0	0±0
	50	0±0	0±0		50	0±0	0±0		50	0±0	0±0
	60	0±0	0±0		60	0±0	0±0		60	0±0	0±0
7000	100	0±0	0±0	7000	100	0±0	0±0	7000	100	0±0	0±0
	30	0±0	0±0		30	0±0	0±0		30	0±0	0±0
	40	0±0	0±0		40	0±0	0±0		40	0±0	0±0
	50	0±0	0±0		50	0±0	0±0		50	0±0	0±0
	60	0±0	0±0		60	0±0	0±0		60	0±0	0±0
		69.8±3.8	49.8±80.8			69.8±3.8	49.8±80.8			49.8±8.7	64.8±18.4
		70.0±3.8	49.8±80.8			70.0±3.8	49.8±80.8			17.8±3.8	80.4±18.4

1区：基本設定				1区：基本設定				1区：基本設定			
回遊数 (Count)	回遊率 (%)	観測回パブル数 (Count±SD)	観測回パブル数 (Count±SD)	回遊数 (Count)	回遊率 (%)	観測回パブル数 (Count±SD)	観測回パブル数 (Count±SD)	回遊数 (Count)	回遊率 (%)	観測回パブル数 (Count±SD)	観測回パブル数 (Count±SD)
1000	30	0±0	0±0	1000	30	0±0	0±0	1000	30	0±0	0±0
	40	0±0	0±0		40	0±0	0±0		40	0±0	0±0
	50	0±0	0±0		50	0±0	0±0		50	0±0	0±0
	60	0±0	0±0		60	0±0	0±0		60	0±0	0±0
	70	0±0	0±0		70	0±0	0±0		70	0±0	0±0
1800	100	0±0	0±0	1800	100	0±0	0±0	1800	100	0±0	0±0
	30	0±0	0±0		30	0±0	0±0		30	0±0	0±0
	40	0±0	0±0		40	0±0	0±0		40	0±0	0±0
	50	0±0	0±0		50	0±0	0±0		50	0±0	0±0
	60	0±0	0±0		60	0±0	0±0		60	0±0	0±0
3000	100	0±0	0±0	3000	100	0±0	0±0	3000	100	0±0	0±0
	30	0±0	0±0		30	0±0	0±0		30	0±0	0±0
	40	0±0	0±0		40	0±0	0±0		40	0±0	0±0
	50	0±0	0±0		50	0±0	0±0		50	0±0	0±0
	60	0±0	0±0		60	0±0	0±0		60	0±0	0±0
5000	100	0±0	0±0	5000	100	0±0	0±0	5000	100	0±0	0±0
	30	0±0	0±0		30	0±0	0±0		30	0±0	0±0
	40	0±0	0±0		40	0±0	0±0		40	0±0	0±0
	50	0±0	0±0		50	0±0	0±0		50	0±0	0±0
	60	0±0	0±0		60	0±0	0±0		60	0±0	0±0
7000	100	0±0	0±0	7000	100	0±0	0±0	7000	100	0±0	0±0
	30	0±0	0±0		30	0±0	0±0		30	0±0	0±0
	40	0±0	0±0		40	0±0	0±0		40	0±0	0±0
	50	0±0	0±0		50	0±0	0±0		50	0±0	0±0
	60	0±0	0±0		60	0±0	0±0		60	0±0	0±0
		70.0±3.8	80.4±19.8			70.0±3.8	80.4±19.8			70.0±3.8	80.4±19.8
		70.0±3.8	80.4±19.8			70.0±3.8	80.4±19.8			70.0±3.8	80.4±19.8

1区：基本設定				1区：基本設定				1区：基本設定			
回遊数 (Count)	回遊率 (%)	観測回パブル数 (Count±SD)	観測回パブル数 (Count±SD)	回遊数 (Count)	回遊率 (%)	観測回パブル数 (Count±SD)	観測回パブル数 (Count±SD)	回遊数 (Count)	回遊率 (%)	観測回パブル数 (Count±SD)	観測回パブル数 (Count±SD)
1000	30	0±0	0±0	1000	30	0±0	0±0	1000	30	0±0	0±0
	40	0±0	0±0		40	0±0	0±0		40	0±0	0±0
	50	0±0	0±0		50	0±0	0±0		50	0±0	0±0
	60	0±0	0±0		60	0±0	0±0		60	0±0	0±0
	70	0±0	0±0		70	0±0	0±0		70	0±0	0±0
1800	100	0±0	0±0	1800	100	0±0	0±0	1800	100	0±0	0±0
	30	0±0	0±0		30	0±0	0±0		30	0±0	0±0
	40	0±0	0±0		40	0±0	0±0		40	0±0	0±0
	50	0±0	0±0		50	0±0	0±0		50	0±0	0±0
	60	0±0	0±0		60	0±0	0±0		60	0±0	0±0
3000	100	0±0	0±0	3000	100	0±0	0±0	3000	100	0±0	0±0
	30	0±0	0±0		30	0±0	0±0		30	0±0	0±0
	40	0±0	0±0		40	0±0	0±0		40	0±0	0±0
	50	0±0	0±0		50	0±0	0±0		50	0±0	0±0
	60	0±0	0±0		60	0±0	0±0		60	0±0	0±0
5000	100	0±0	0±0	5000	100	0±0	0±0	5000	100	0±0	0±0
	30	0±0	0±0		30	0±0	0±0		30	0±0	0±0
	40	0±0	0±0		40	0±0	0±0		40	0±0	0±0
	50	0±0	0±0		50	0±0	0±0		50	0±0	0±0
	60	0±0	0±0		60	0±0	0±0		60	0±0	0±0
7000	100	0±0	0±0	7000	100	0±0	0±0	7000	100	0±0	0±0
	30	0±0	0±0		30	0±0	0±0		30	0±0	0±0
	40	0±0	0±0		40	0±0	0±0		40	0±0	0±0
	50	0±0	0±0		50	0±0	0±0		50	0±0	0±0
	60	0±0	0±0		60	0±0	0±0		60	0±0	0±0
		71.8±3.7	80.4±19.8			71.8±3.7	80.4±19.8			71.8±3.7	80.4±19.8
		71.8±3.7	80.4±19.8			71.8±3.7	80.4±19.8			71.8±3.7	80.4±19.8

1区：基本設定				1区：基本設定				1区：基本設定			
回遊数 (Count)	回遊率 (%)	観測回パブル数 (Count±SD)	観測回パブル数 (Count±SD)	回遊数 (Count)	回遊率 (%)	観測回パブル数 (Count±SD)	観測回パブル数 (Count±SD)	回遊数 (Count)	回遊率 (%)	観測回パブル数 (Count±SD)	観測回パブル数 (Count±SD)
1000	30	0±0	0±0	1000	30	0±0	0±0	1000	30	0±0	0±0
	40	0±0	0±0		40	0±0	0±0		40	0±0	0±0
	50	0±0	0±0		50	0±0	0±0		50	0±0	0±0
	60	0±0	0±0		60	0±0	0±0		60	0±0	0±0
	70	0±0	0±0		70	0±0	0±0		70	0±0	0±0
1800	100	0±0	0±0	1800	100	0±0	0±0	1800	100	0±0	0±0
	30	0±0	0±0		30	0±0	0±0		30	0±0	0±0
	40	0±0	0±0		40	0±0	0±0		40	0±0	0±0
	50	0±0	0±0		50	0±0	0±0		50	0±0	0±0
	60	0±0	0±0		60	0±0	0±0		60	0±0	0±0
3000	100	0±0	0±0	3000	100	0±0	0±0	3000	100	0±0	0±0
	30	0±0	0±0		30	0±0	0±0		30	0±0	0±0
	40	0±0	0±0		40	0±0	0±0		40	0±0	0±0
	50	0±0	0±0		50	0±0	0±0		50	0±0	0±0
	60	0±0	0±0		60	0±0	0±0		60	0±0	0±0
5000	100	0±0	0±0	5000	100	0±0	0±0	5000	100	0±0	0±0
	30	0±0	0±0		30	0±0	0±0		30	0±0	0±0
	40	0±0	0±0		40	0±0	0±0		40	0±0	0±0
	50	0±0	0±0		50	0±0	0±0		50	0±0	0±0
	60	0±0	0±0		60	0±0	0±0		60	0±0	0±0
7000	100	0±0	0±0	7000	100	0±0	0±0	7000	100	0±0	0±0
	30	0±0	0±0		30	0±0	0±0		30	0±0	0±0
	40	0±0	0±0		40	0±0	0±0		40	0±0	0±0
	50	0±0	0±0		50	0±0	0±0		50	0±0	0±0
	60	0±0	0±0		60	0±0	0±0		60	0±0	0±0
		71.8±3.7	80.4±19.8			71.8±3.7	80.4±19.8			71.8±3.7	80.4±19.8
		71.8±3.7	80.4±19.8			71.8±3.7	80.4±19.8			71.8±3.7	80.4±19.8

1区：基本設定				1区：基本設定				1区：基本設定			
回遊数 (Count)	回遊率 (%)	観測回パブル数 (Count±SD)	観測回パブル数 (Count±SD)	回遊数 (Count)	回遊率 (%)	観測回パブル数 (Count±SD)	観測回パブル数 (Count±SD)	回遊数 (Count)	回遊率 (%)	観測回パブル数 (Count±SD)	観測回パブル数 (Count±SD)
1000	30	0±0	0±0	1000	30	0±0	0±0	1000	30	0±0	0±0
	40	0±0	0±0		40	0±0	0±0		40	0±0	0±0
	50	0±0	0±0		50	0±0	0±0		50	0±0	0±0
	60	0±0	0±0		60	0±0	0±0		60	0±0	0±0
	70	0±0	0±0		70	0±0	0±0		70	0±0	0±0
1800	100	0±0	0±0	1800	100	0±0	0±0	1800	100	0±0	0±0
	30	0±0	0±0		30	0±0	0±0		30	0±0	0±0
	40	0±0	0±0		40	0±0	0±0		40	0±0	0±0
	50	0±0	0±0		50	0±0	0±0		50	0±0	0±0
	60	0±0	0±0		60	0±0	0±0		60	0±0	0±0
3000	100	0±0	0±0	3000	100	0±0	0±0	3000	100	0±0	0±0
	30	0±0	0±0		30	0±0	0±0		30	0±0	0±0
	40	0±0	0±0		40	0±0	0±0		40	0±0	0±0
	50	0±0	0±0		50	0±0	0±0		50	0±0	0±0
	60	0±0	0±0		60	0±0	0±0		60	0±0	0±0
5000	100	0±0	0±0	5000	100	0±0	0±0	5000	100	0±0	0±0
	30	0±0	0±0		30	0±0	0±0		30	0±0	0±0
	40	0±0	0±0		40	0±0	0±0		40	0±0	0±0
	50	0±0	0±0		50	0±0	0±0		50	0±0	0±0
	60	0±0	0±0		60	0±0	0±0		60	0±0	0±0
7000	100	0±0	0±0	7000	100	0±0	0±0	7000	100	0±0	0±0
	30	0±0	0±0		30	0±0	0±0		30	0±0	0±0
	40	0±0	0±0		40	0±0	0±0		40	0±0	0±0
	50	0±0	0±0		50	0±0	0±0		50	0±0	0±0
	60	0±0	0±0		60	0±0	0±0		60	0±0	0±0
		71.8±3.7	80.4±19.8			71.8±3.7	80.4±19.8			71.8±3.7	80.4±19.8
		71.8±3.7	80.4±19.8			71.8±3.7	80.4±19.8			71.8±3.7	80.4±19.8

[illegible]

1978-1988 1998		1998
総重量 (gram)	質量パーセント (mass-%)	質量パーセント (mass-%)
1000	20	0.0 ± 0.0
	40	0.0 ± 0.0
	60	0.0 ± 0.0
	80	0.0 ± 0.0
	100	0.0 ± 0.0
1800	20	0.0 ± 0.0
	40	0.0 ± 0.0
	60	0.0 ± 0.0
	80	0.0 ± 0.0
	100	0.0 ± 0.0
3000	20	0.0 ± 0.0
	40	0.0 ± 0.0
	60	0.0 ± 0.0
	80	0.0 ± 0.0
	100	0.0 ± 0.0
3800	20	0.0 ± 0.0
	40	0.0 ± 0.0
	60	0.0 ± 0.0
	80	0.0 ± 0.0
	100	0.0 ± 0.0
5000	20	0.0 ± 0.0
	40	0.0 ± 0.0
	60	0.0 ± 0.0
	80	0.0 ± 0.0
	100	0.0 ± 0.0

試験数 (n)	同意率 (%)	SPY 100% 原価率パナル表 (mean±SD)	n=1 検査側パナル表 (mean±SD)
1000	20	0±0	0±0
	40	0±0	0±0
	60	0±0	0±0
	80	0±0	0±0
	100	0±0	0±0
1500	20	0±0	0±0
	40	0±0	0±0
	60	0±0	0±0
	80	0±0	0±0
	100	0±0	0±0
2000	20	0±0	0±0
	40	0±0	0±0
	60	0±0	0±0
	80	0±0	0±0
	100	0±0	0±0
2500	20	1.2±0.7	0±0
	40	1.3±0.7	0±0
	60	1.1±1.3	0±0
	80	0±0	0±0
	100	10±0.0	25.5±0.0
3000	20	0±0	0±0
	40	0±0	0±0
	60	0±0	0±0
	80	4.9±0.4	71.8±1.0
	100	11±0.3	80.1±1.0

【例 1】 分散度 Ⅱ		【例 2】	
試験回数 (Case)	問正率	原価調査バブル数 (Score調査?)	巻込み調査バブル数 (Score調査?)
1000	20	0±0.0	0±0.0
	40	0±0.0	0±0.0
	60	0±0.0	0±0.0
	80	0±0.0	0±0.0
	100	0±0.0	0±0.0
1500	20	0±0.0	0±0.0
	40	0±0.0	0±0.0
	60	0±0.0	0±0.0
	80	0±0.0	0±0.0
	100	0±0.0	0±0.0
2000	20	0±0.0	0±0.0
	40	0±0.0	0±0.0
	60	0±0.0	0±0.0
	80	0±0.0	0±0.0
	100	0±0.0	0±0.0
2500	20	0±0.0	0±0.0
	40	0±0.0	0±0.0
	60	0±0.0	0±0.0
	80	4.5±0.0	0±0.0
	100	10±0.0	0±0.0, 7
3000	20	0±0.0	0±0.0
	40	0±0.0	0±0.0
	60	0±0.0	4.0±0.0
	80	7.0±0.0	4.0±0.0
	100	10.0±0.0	6.0±0.0

		17. カラ数表 11		12	
回数表	回数半	回数表17.5表	回数表17.5表	回数表17.5表	回数表17.5表
1000	30	0.0	0.0	0.0	0.0
	40	0.0	0.0	0.0	0.0
	50	0.0	0.0	0.0	0.0
	60	0.0	0.0	0.0	0.0
	70	0.0	0.0	0.0	0.0
	80	0.0	0.0	0.0	0.0
	90	0.0	0.0	0.0	0.0
	100	0.0	0.0	0.0	0.0
1500	30	0.0	0.0	0.0	0.0
	40	0.0	0.0	0.0	0.0
	50	0.0	0.0	0.0	0.0
	60	0.0	0.0	0.0	0.0
	70	0.0	0.0	0.0	0.0
	80	0.0	0.0	0.0	0.0
	90	0.0	0.0	0.0	0.0
	100	0.0	0.0	0.0	0.0
2000	30	0.0	0.0	0.0	0.0
	40	0.0	0.0	0.0	0.0
	50	0.0	0.0	0.0	0.0
	60	0.0	0.0	0.0	0.0
	70	0.0	0.0	0.0	0.0
	80	0.0	0.0	0.0	0.0
	90	0.0	0.0	0.0	0.0
	100	0.0	0.0	0.0	0.0
2500	30	0.0	0.0	0.0	0.0
	40	0.0	0.0	0.0	0.0
	50	0.0	0.0	0.0	0.0
	60	0.0	0.0	0.0	0.0
	70	0.0	0.0	0.0	0.0
	80	0.0	0.0	0.0	0.0
	90	0.0	0.0	0.0	0.0
	100	0.0	0.0	0.0	0.0
3000	30	0.0	0.0	0.0	0.0
	40	0.0	0.0	0.0	0.0
	50	0.0	0.0	0.0	0.0
	60	0.0	0.0	0.0	0.0
	70	0.0	0.0	0.0	0.0
	80	0.0	0.0	0.0	0.0
	90	0.0	0.0	0.0	0.0
	100	0.0	0.0	0.0	0.0

		1977 年 3 月 31 日現在		1977 年 3 月 31 日現在	
四半期別	四半期	原価額(百万円)	売上高(百万円)	原価額(百万円)	売上高(百万円)
1977	1Q	20	0 円 0 角	0 円 0 角	0 円 0 角
	2Q	40	0 円 0 角	0 円 0 角	0 円 0 角
	3Q	60	0 円 0 角	0 円 0 角	0 円 0 角
	4Q	80	0 円 0 角	0 円 0 角	0 円 0 角
	1Q	100	0 円 0 角	0 円 0 角	0 円 0 角
1978	1Q	40	0 円 0 角	0 円 0 角	0 円 0 角
	2Q	60	0 円 0 角	0 円 0 角	0 円 0 角
	3Q	80	0 円 0 角	0 円 0 角	0 円 0 角
	4Q	100	0 円 0 角	0 円 0 角	0 円 0 角
	1Q	20	0 円 0 角	0 円 0 角	0 円 0 角
1979	1Q	20	0 円 0 角	0 円 0 角	0 円 0 角
	2Q	40	0 円 0 角	0 円 0 角	0 円 0 角
	3Q	60	0 円 0 角	0 円 0 角	0 円 0 角
	4Q	80	0 円 0 角	0 円 0 角	0 円 0 角
	1Q	100	0 円 0 角	0 円 0 角	0 円 0 角
1980	1Q	20	0 円 0 角	0 円 0 角	0 円 0 角
	2Q	40	0 円 0 角	0 円 0 角	0 円 0 角
	3Q	60	0 円 0 角	0 円 0 角	0 円 0 角
	4Q	80	0 円 0 角	0 円 0 角	0 円 0 角
	1Q	100	0 円 0 角	0 円 0 角	0 円 0 角
1981	1Q	20	0 円 0 角	0 円 0 角	0 円 0 角
	2Q	40	0 円 0 角	0 円 0 角	0 円 0 角
	3Q	60	0 円 0 角	0 円 0 角	0 円 0 角
	4Q	80	0 円 0 角	0 円 0 角	0 円 0 角
	1Q	100	0 円 0 角	0 円 0 角	0 円 0 角

[illegible]

177. カナダ産 魚		単位
品名	数量	数量
品名	数量	数量
1770	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
1800	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
1830	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
1860	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
1890	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
1920	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
1950	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
1980	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
2010	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
2040	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
2070	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
2100	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
2130	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
2160	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
2190	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
2220	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
2250	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
2280	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
2310	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
2340	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
2370	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
2400	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
2430	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
2460	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
2490	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
2520	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
2550	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
2580	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
2610	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
2640	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
2670	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
2700	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
2730	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
2760	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
2790	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
2820	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
2850	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
2880	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
2910	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
2940	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
2970	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
3000	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
3030	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
3060	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
3090	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
3120	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
3150	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
3180	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
3210	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
3240	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
3270	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
3300	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
3330	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
3360	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
3390	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
3420	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
3450	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
3480	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
3510	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
3540	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
3570	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
3600	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
3630	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
3660	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
3690	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
3720	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
3750	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
3780	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
3810	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
3840	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
3870	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
3900	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
3930	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
3960	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
3990	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
4020	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
4050	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
4080	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
4110	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
4140	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
4170	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
4200	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
4230	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
4260	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
4290	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
4320	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
4350	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
4380	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
4410	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
4440	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
4470	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
4500	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
4530	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
4560	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
4590	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
4620	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
4650	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
4680	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
4710	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
4740	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
4770	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
4800	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
4830	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
4860	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
4890	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
4920	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
4950	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50
4980	30	0.50
	40	0.50
	50	0.50
	100	0.50
	100	0.50</

[illegible]

1000		2000		4000		8000	
標準偏差 (mm)	標準偏差 (%)	標準偏差 (mm)	標準偏差 (%)	標準偏差 (mm)	標準偏差 (%)	標準偏差 (mm)	標準偏差 (%)
1000	20	0.±0	0.±0	20	0.±0	40	0.±0
	40	0.±0	0.±0	40	0.±0	80	0.±0
	60	0.±0	0.±0	60	0.±0	120	0.±0
	80	0.±0	0.±0	80	0.±0	160	0.±0
	100	0.±0	0.±0	100	0.±0	200	0.±0
2000	20	0.±0	0.±0	20	0.±0	40	0.±0
	40	0.±0	0.±0	40	0.±0	80	0.±0
	60	0.±0	0.±0	60	0.±0	120	0.±0
	80	0.±0	0.±0	80	0.±0	160	0.±0
	100	0.±0	0.±0	100	0.±0	200	0.±0
4000	20	0.±0	0.±0	20	0.±0	40	0.±0
	40	0.±0	0.±0	40	0.±0	80	0.±0
	60	0.±0	0.±0	60	0.±0	120	0.±0
	80	0.±0	0.±0	80	0.±0	160	0.±0
	100	0.±0	0.±0	100	0.±0	200	0.±0
8000	20	0.±0	0.±0	20	0.±0	40	0.±0
	40	0.±0	0.±0	40	0.±0	80	0.±0
	60	0.±0	0.±0	60	0.±0	120	0.±0
	80	0.±0	0.±0	80	0.±0	160	0.±0
	100	0.±0	0.±0	100	0.±0	200	0.±0

177. ガラス管、円		mm	
外径寸法 (mm)	厚さ (mm)	重量1mの長さ (g/mm)	重量1mの長さ (g/mm)
1000	20	0±0.5	0±0.0
	40	0±0.0	0±0.0
	60	0±0.0	0±0.0
	80	0±0.0	0±0.0
	100	0±0.0	0±0.0
	120	0±0.0	0±0.0
1800	20	0±0.0	0±0.0
	40	0±0.0	0±0.0
	60	0±0.0	0±0.0
	80	0±0.0	0±0.0
	100	0±0.0	0±0.0
	120	0±0.0	0±0.0
2000	20	0±0.0	0±0.0
	40	0±0.0	0±0.0
	60	0±0.0	0±0.0
	80	0±0.0	0±0.0
	100	0±0.0	0±0.0
	120	0±0.0	0±0.0
2800	20	0±0.0	0±0.0
	40	0±0.0	0±0.0
	60	0±0.0	0±0.0
	80	0±0.0	0±0.0
	100	0±0.0	0±0.0
	120	0±0.0	0±0.0
3000	20	0±0.0	0±0.0
	40	0±0.0	0±0.0
	60	0±0.0	0±0.0
	80	0±0.0	0±0.0
	100	0±0.0	0±0.0
	120	0±0.0	0±0.0

[illegible]

15Fr 温度 37℃ n=5				17Fr 温度 37℃ n=5				19Fr 温度 37℃ n=5			
回転数 (rpm)	閉塞率 (%)	脱血側バブル数 (mean±SD)	逆血側バブル数 (mean±SD)	回転数 (rpm)	閉塞率 (%)	脱血側バブル数 (mean±SD)	逆血側バブル数 (mean±SD)	回転数 (rpm)	閉塞率 (%)	脱血側バブル数 (mean±SD)	逆血側バブル数 (mean±SD)
1000	20	0±0	0±0	1000	20	0±0	0±0	1000	20	0±0	0±0
	40	0±0	0±0		40	0±0	0±0		40	0±0	0±0
	60	0±0	0±0		60	0±0	0±0		60	0±0	0±0
	80	0±0	0±0		80	0±0	0±0		80	0±0	0±0
	100	0±0	0±0		100	0±0	0±0		100	0±0	0±0
1500	20	0±0	0±0	1500	20	0±0	0±0	1500	20	0±0	0±0
	40	0±0	0±0		40	0±0	0±0		40	0±0	0±0
	60	0±0	0±0		60	0±0	0±0		60	0±0	0±0
	80	0±0	0±0		80	0±0	0±0		80	0±0	0±0
	100	0±0	0±0		100	0±0	0±0		100	0±0	0±0
2000	20	0±0	0±0	2000	20	0±0	0±0	2000	20	0±0	0±0
	40	0±0	0±0		40	0±0	0±0		40	0.4±0.5	0±0
	60	0±0	0±0		60	0±0	0±0		60	0±0	0±0
	80	0±0	0±0		80	0±0	0±0		80	0±0	0±0
	100	0±0	0±0		100	0±0	0±0		100	0±0	0±0
2500	20	0±0	0±0	2500	20	0±0	0±0	2500	20	0±0	0±0
	40	0±0	0±0		40	0±0	0±0		40	0±0	0±0
	60	0±0	0±0		60	0±0	0±0		60	0±0	0±0
	80	6.6±3.8	0±0		80	0±0	0±0		80	0±0	0±0
	100	10.4±2.6	0.8±0.7		100	0.6±0.8	1.2±1.5		100	0.8±1.2	0±0
3000	20	0±0	0±0	3000	20	0.6±0.5	0±0	3000	20	0.4±0.5	0±0
	40	0±0	0±0		40	0.4±0.5	0±0		40	0±0	0±0
	60	0±0	0±0		60	0.2±0.4	0±0		60	1±0	0.8±0.7
	80	72.4±2.3	50.4±19.9		80	70.2±6.8	91.2±8.4		80	48.8±9.4	78.2±5.9
	100	17.5±2.4	67.4±6.6		100	25.5±4.9	87.4±7.8		100	22.6±4.1	55.6±2.2

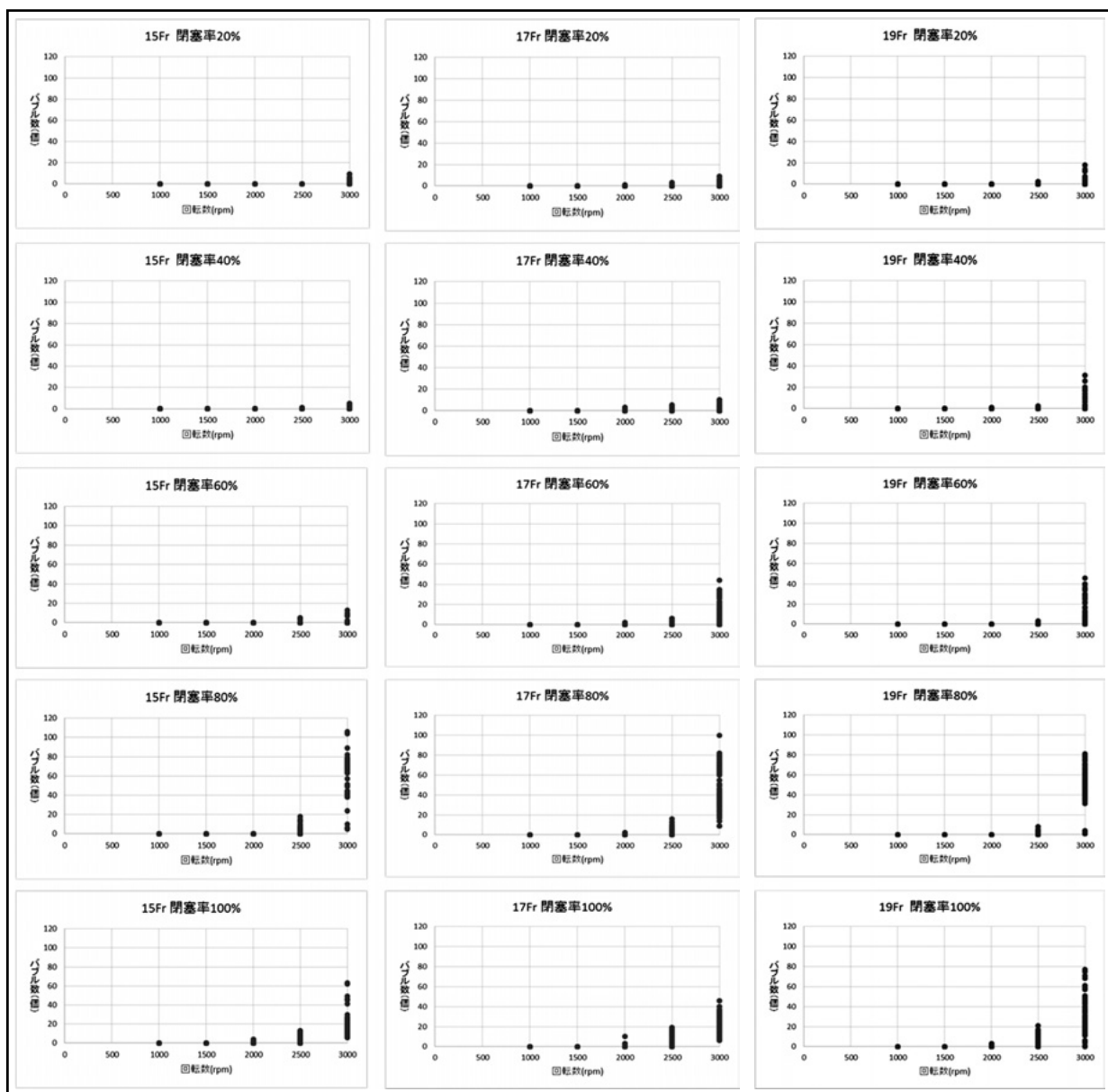


図 3 回転数とバブル数の関係

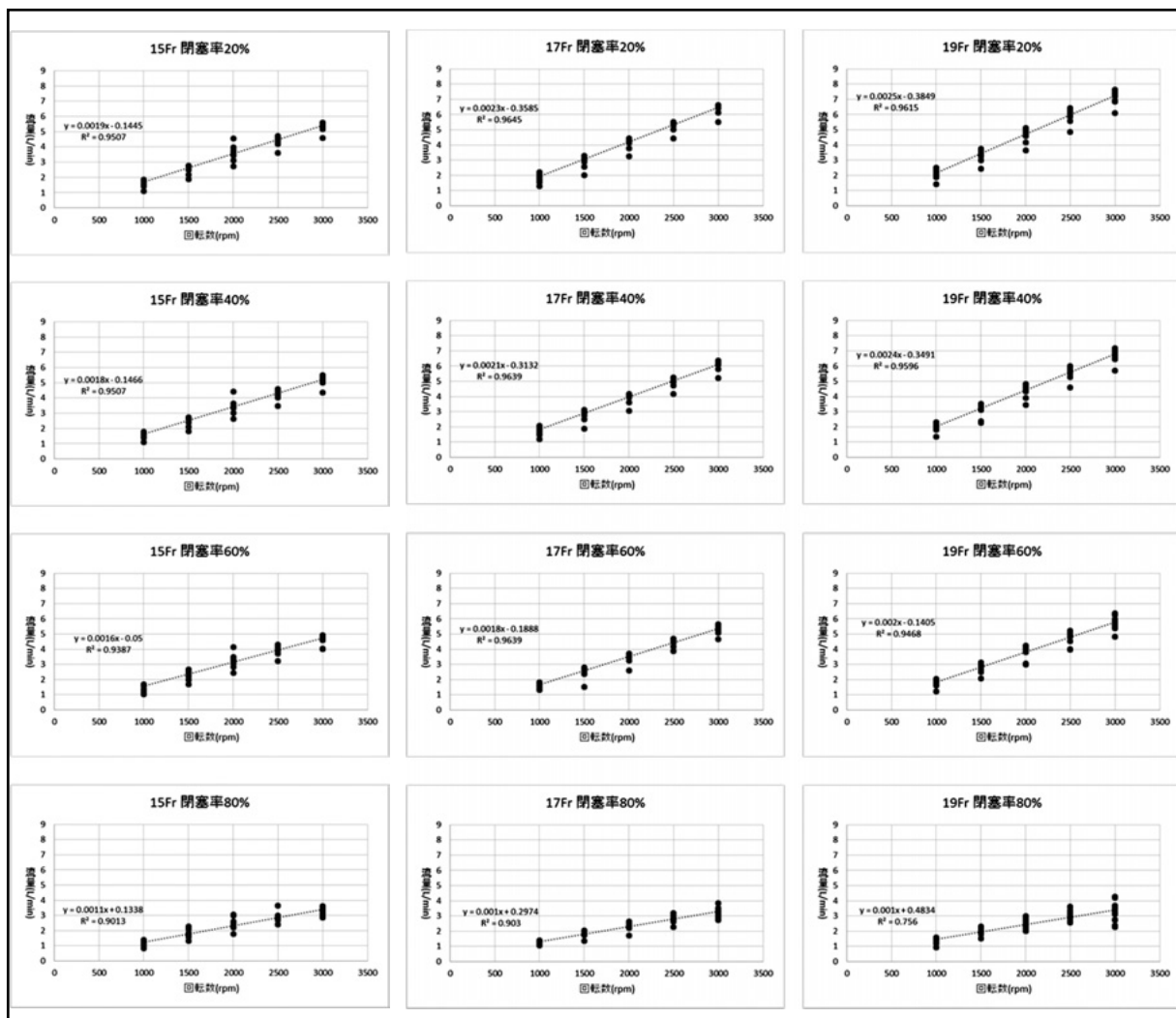


図 4 回転数と模擬血液流量の関係

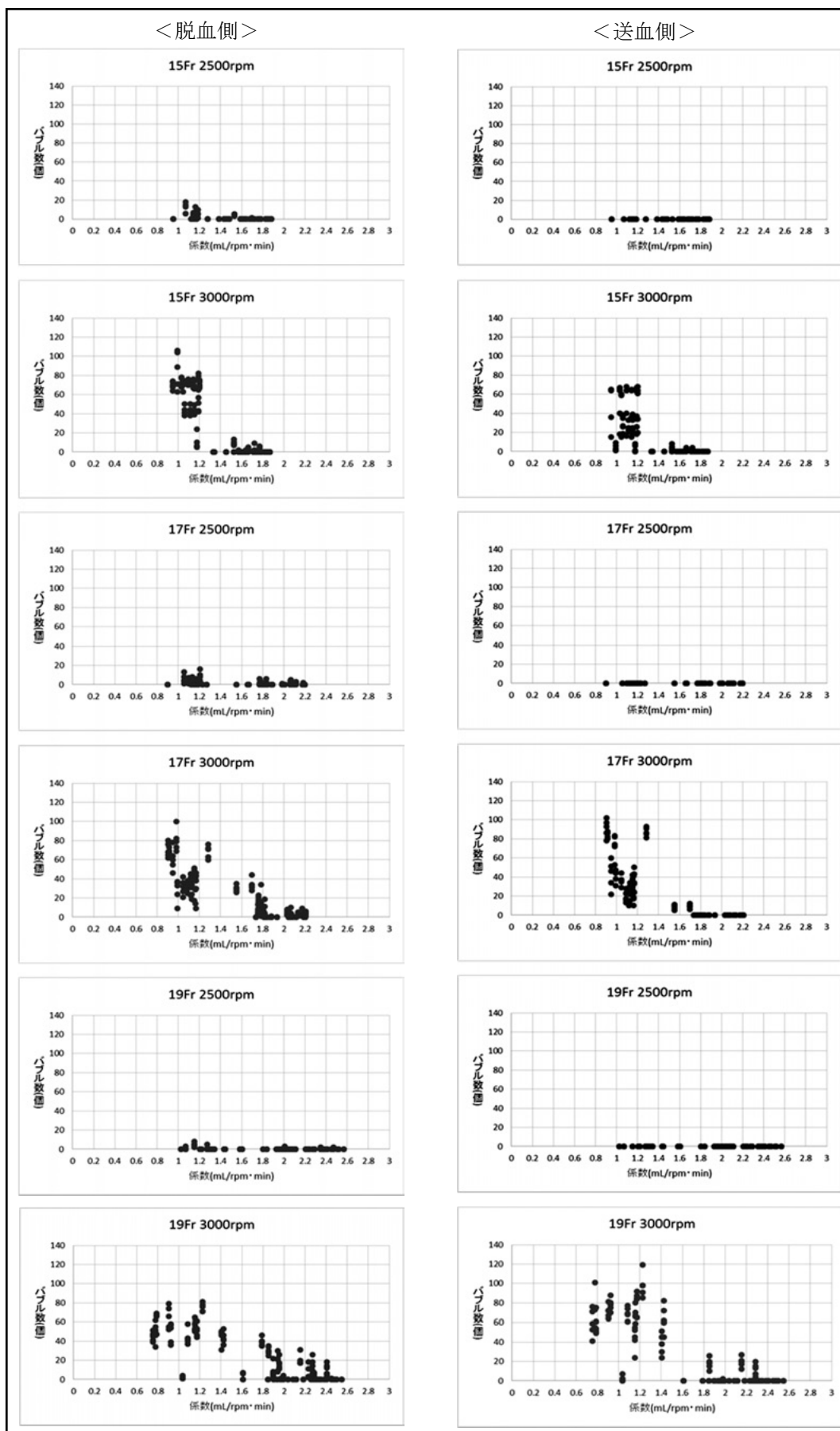


図5 係数とバブル数の関係

られるもののバブルの発生する係数範囲については同値を示す結果となった。

4. 各種条件が係数範囲に与える影響

図5で求めたバブル数が多く発生する係数範囲について、基本設定、ガス条件（流量、 FiO_2 ）、温度変化が係数範囲に影響を及ぼさないか統計学的処理（ $p < 0.05$, Tukey-Kramer法）を行ったところ温度変化でのみ若干の有意差を認める結果となった。

IV. 考察

これまでPCPS使用中のキャビテーションによるマイクロバブルの発生については、様々な報告がなされ⁶⁾⁷⁾、気泡の発生対策⁸⁾⁹⁾やその危険性¹⁰⁾¹¹⁾についても検討されてきた。しかし、その原因について多くの場合、脱血不良や回路閉塞など原因は明らかであるが、これまで具体的に指標となる検討は少なかった。

今回の調査結果では、まず回転数と閉塞率の関係性（図3）においてバブル数のバラつきと閉塞率による分布に一部規則性が認められなかった。しかし、模擬血液流量と回転数から求めた係数とバブルの関係（図5）においては、閉塞率や送血管のサイズに関係なく統計学上

（ $p < 0.05$, Tukey-Kramer法）の有意差は認められなかった。しかし、唯一、係数と温度変化の関係においては若干の有意差を認めた。

この理由として、著者らが行った臨床状態を模擬した水系実験では、まず図3の閉塞率を変化させたときに高い閉塞率で規則性が認められなかったことは、閉塞率80%では緩やかではあるが遠心ポンプへ模擬血液が送られるのに対し、閉塞率100%では一時的に流れが遮断される。この間に細かい気泡は凝集し一塊の大きなバブルとなることでバブル数が減少したと考えられた。また、バブル数にバラつきがみられたのは、通常液体は、低温状態では粘性係数が大きくなり相対的にキャビテーションが起りやすくなるという報告がある¹²⁾。このことから低温状態（10℃、20℃）においては、模擬血液

の粘性変化が大きく影響したと考えられた。

一方、各種条件が係数範囲に与える影響について、温度変化のみで差がみられる点に関しても温度変化による粘性変化が原因と考えられた。そこで温度条件の中でも低体温（10℃、20℃）を除いた、臨床上起こり得る条件（30℃、36℃、37℃）のみ再度統計学的処理（ $p < 0.05$, Tukey-Kramer法）を行ってみると有意差は認められず係数が臨床使用上問題ないことが示された。

ここで、この係数を用いてPCPSにおけるキャビテーション防止を目的とした早見表を作成した。

1. 至適灌流量を求める早見表

ポンプ回転数（rpm）と係数（ $\text{mL/rpm} \cdot \text{min}$ ）から至適灌流量を求める早見表を図6に示す。これは、係数の中でも最もバブル数が集中した最大値0.8（赤色）、最小値1.4（黄色）と実験中、各送血管の太さ（Fr）別のうち気泡計測器にて1つでもバブルが認められた時の値（青色）の3つの係数と回転数から理論値を求め作図した。

（ただし、条件として非臨床的な条件を省いた、血液流量温度30℃～37℃、閉塞率0～80%以内の場合に限る。）

使用方法としては、回転数をもとに流量を見た場合、赤色と黄色の直線で囲まれた範囲にあればバブルの発生頻度が非常に高い状態であり、黄色と青色に囲まれた範囲にあればバブルの発生が極めて低い低危険領域となる。また、青色の直線より上に行けば安全域になることが容易に推定できる。

本研究で導き出された理論値表は新規のデバイスを必要とせず、通常モニタリングされている回転数と流量のコントロールによりキャビテーションによる気泡発生を抑止できる可能性がある点で有用であると考えている。ただし遠心ポンプの径により係数は変動するため、他の遠心ポンプでは係数を測定しなおす必要がある。

また、今回はグリセリン水溶液を用いた水系実験であったため血液でも再現性が得られるか今後更なる検討が必要であると考え。

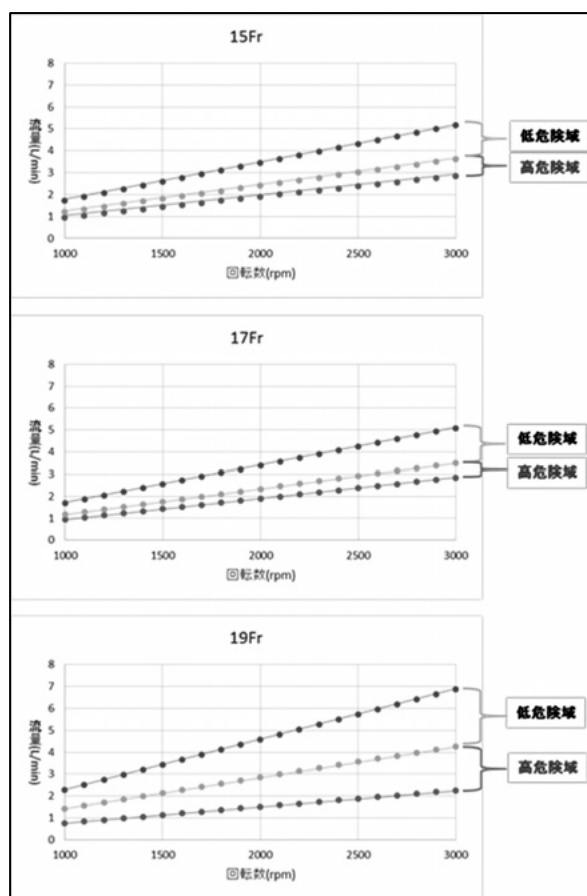


図6 早見表

V. 結語

1. 臨床的な条件であればキャビテーションによる気泡発生と PCPS の設定条件との関連性は係数($L/rpm \cdot min$)を用いることで表すことが可能である。
2. 今回提案した早見表により、個々の患者の状態に合わせてキャビテーションによる気泡発生の危険性を予測することが可能である。
3. 実験は、水系実験のため今後さらなる検討が必要である。

VI. 研究協力者

峰松佑輔・国立病院機構大阪医療センター・臨床工学技士

宮川幸恵・国立病院機構大阪医療センター・臨床工学技士

湊拓巳・国立病院機構大阪医療センター・臨床工学技士

池宮裕太・国立病院機構大阪医療センター・臨床工学技士

柴田純一・国立病院機構大阪医療センター・臨床工学技士

VII. 参考文献

- 1) 笹山幸治:人工心肺器材と Gaseous Microemboli の予防.人工臓器 2013;Vol.42,No.3:236-240
- 2) 日本機械学会(編):機械工学便覧 基礎編 α 4 流体力学.東京.丸善出版;2006.136-143
- 3) CE Brennen:Cavitation and Bubble Dynamics.New York.Oxford University Press;1995.35-7
- 4) 安達秀雄,百瀬直樹,又吉盛博:人工心肺ハンドブック.東京.中外医学社;2004.122-124
- 5) 倉島直樹,芝本隆,小堀昭:遠心ポンプ送血におけるエア混入時の安全対策.体外循環技術 2008;Vol.35,No.4:416-419
- 6) Takahashi M:Zeta potential of microbubbles in aqueous solutions.Journal of Physical Chemistry B 2005;109:21858-21864
- 7) 岩田浩一,阿部敬二郎,宇都宮精治郎:PCPS の状態の違いによる気泡発生の実験的検討.体外循環技術 2004;Vol.31,No.1:68-70
- 8) 加藤優,長谷川武生,前中則武,ほか:経皮的心肺補助法における Bubble-Trap の有効性.体外循環技術 2005;Vol.32,No.4:395-399
- 9) 福長一義,舟久保昭夫,樋上哲哉,ほか:膜型人工肺が有する Bubble Trap Performance の測定.人工臓器 2000;Vol.29,No.1:93-98
- 10) 又吉徹:体外循環中の微小気泡が与える人体への影響について.体外循環技術 2012;Vol.39,No.3:289
- 11) Claus M.Muth,Erik S.Shank:GAS EMBOLISM.The New England Journal of

Medicine 2000;Vol.342,No.7:476-482

- 12) 江連俊樹,三宅康洋,飛田昭,ほか:液中渦キャ
ビテーションに関する基礎的研究.JAEA-
Research 2012:005:1-49