genotype 1 [2]. PVB19 has been shown to cause erythema infectiosum in children as well as acute red cell aplasia in patients who have conditions causing hematopoietic stress, such as hemolytic anemia; this virus has also been implicated in the pathogenesis of rheumatic arthritis, myocarditis, nephritis, fulminant liver disease, and many other conditions [3]. In HIV-1-positive patients, PVB19 may persistently infect erythroid precursor cells, evade elimination by the immune system, and cause transfusion-dependent pure red cell anemia (PRCA) [4]. PVB19-related anemia can be resolved by treatment with intravenous immunoglobulin (Ig) [5]. However, this treatment often has a transient beneficial effect, and AIDS patients might experience a relapse of anemia. Therefore, AIDS patients may require periodic administration of intravenous Ig or blood transfusions. In recent years, some reports have shown that complete remission of PVB19-associated PRCA can be achieved by treating patients with HAART [6–8]. Although patients with HIV-1 infection show high seroprevalence of PVB19 [9], few reports have been published on primary or persistent PVB19 infection, particularly PVB19-related IRIS, in HIV-1-infected patients. In this report, we describe the case of a man with AIDS who presented with chronic PVB19-induced PRCA and IRIS after undergoing HAART. We focus on the relationship between the clinical presentation and immunological status in this condition.

Case report

A 54-year-old HIV-1-positive man visited our hospital in May 2006. He had been diagnosed with *Pneumocystis jiroveci* pneumonia and treated with sulfamethoxazole/trimethoprim in February 2006. His initial CD4 cell count was 35 cells/μl, and the plasma HIV-1 RNA level was 250,000 copies/ml. The results of other laboratory analyses were normal, except for the presence of slight anemia (hemoglobin level 11.5 g/dl). He reported that he had traveled abroad to Southeast Asia for personal reasons.

In November 2006, he re-visited our hospital, and his hemoglobin level had decreased to 7.7 g/dl. He did not show any other symptoms, such as fever, rash, or arthralgia, or any signs of cardiac, renal, or hepatic disorders. He did not report any direct contact with patients having erythema infectiosum. Two weeks later, he experienced dyspnea and was hospitalized immediately. Severe anemia was detected (hemoglobin 5.3 g/dl), and blood transfusions were performed (Fig. 1; Table 1). Gastrointestinal bleeding and hemolytic anemia were ruled out. PVB19 infection was suspected, and an immunoassay [Parvo B19 IgM-enzyme immunoassay (EIA); "SEIKEN," Denka Seiken, Tokyo, Japan] revealed anti-PVB19 IgM antibodies in the serum.

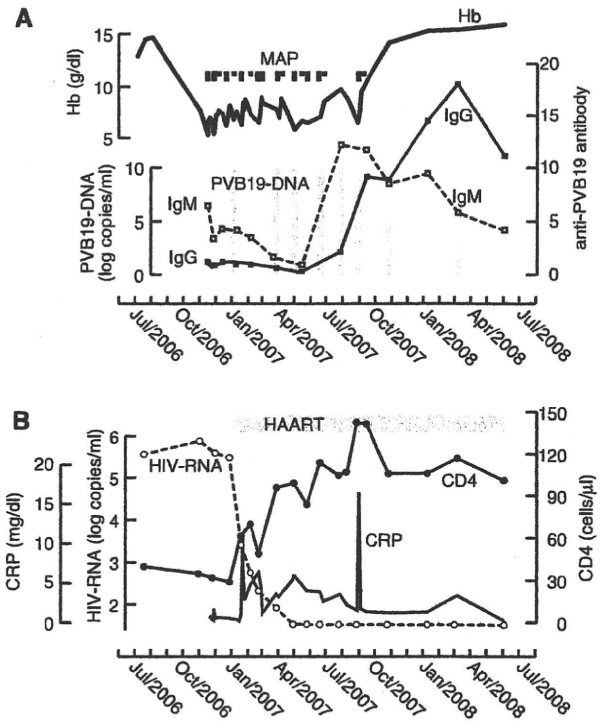

Fig. 1 The patient's clinical course with the changes in the hemoglobin levels and immunological status at the primary and persistent PVB19 infection and at the resolution of PRCA. **a** The *upper solid line* shows the time course of changes in the hemoglobin (Hb) level. The *closed boxes* indicate transfusion of 2 U of packed red blood cells. The *lower solid line* and the *broken line* represent the EIA indices of anti-PVB19 IgG and IgM antibodies, respectively. The *gray bars* show the concentration of serum PVB19-DNA. **b** Time course of changes in the CD4 cell count, plasma HIV-1-RNA levels, and CRP concentrations as well as the duration of HAART are shown

A qualitative polymerase chain reaction (PCR) analysis performed at BML Inc. (Tokyo, Japan) revealed the presence of erythrovirus DNA in the serum. The commercial assays for PVB19-DNA can detect erythrovirus DNA, including the DNA of the newly described erythrovirus variants (genotype 2 and 3) [2]. Quantitative assessment, i.e., real-time PCR analysis, was not performed at this point. The anti-PVB19 IgG antibody index assessed using Parvo B19 IgG-EIA (Seiken, Denak Seiken) was borderline positive (0.92). Examination of a bone marrow aspirate revealed an aplastic marrow (myeloid/erythroid ratio 63:1). Neither parasites nor hemophagocytic cells were found in the aspirate. Although typical giant proerythroblasts were not observed, acute PRCA caused by primary PVB19 infection was diagnosed. The patient was transfused with 6–8 U of blood per month. The anti-PVB19 IgG antibody index gradually reduced and changed from borderline-positive to negative, and the anemia did not improve; these findings indicated a transition from primary PVB19 infection to chronic and persistent infection. Intravenous Ig

Table 1 Summarizing conditions of PVB19 infection, anemia, and immunological findings

Date (year/month)	PVB19 infection	Anemia	Decision of EIA		PVB19-DNA (log copies/ml)	CD4 cell count	HAART
			PVB19-IgG	PVB19-IgM			
2006/11	Primary infection	Acute anemia	+−	+	ND	35	−
2007/1	Persistent infection with high level viremia	Chronic anemia	−	+	10	29	−
2007/9	IRIS	Deterioration	+	+	9	142	+
2007/11	Low level viremia	Remission of PRCA	+	+	3–5	106	+

ND not determined

therapy was not administered because it is an expensive procedure.

From January 2007, HAART with tenofovir, emtricitabine, and efavirenz were initiated. The patient's CD4 cell count gradually increased, and his HIV-1 viral load became undetectable after May 2007. At the beginning of July 2007, the CD4 cell count had increased to 105 cells/μl, and seroconversion of IgG antibody was observed. Although the serum PVB19-DNA level was unchanged, the hemoglobin level increased to 9.8 g/dl, and the periodical blood transfusions were discontinued.

Two months after the last transfusion, the patient experienced episodes of dizziness and visited our hospital. His hemoglobin level rapidly deteriorated to 6.5 g/dl, and blood transfusion was repeated. The serum PVB19 load had reduced tenfold (from 10^{10} to 10^{9} copies/ml). After 3 days, he developed fever and neutropenia (1,100 cells/μl), and circulating atypical lymphocytes were detected. Serum biochemical assessments showed elevated concentrations of lactate dehydrogenase (LDH) (395 IU/l) and C-reactive protein (CRP) (16.47 mg/dl). No other symptoms such as rash or arthralgia and no signs of cardiac, renal, or hepatic disorders were observed. The patient's symptoms disappeared, the abnormal test results reverted to normal within a few days, and the anemia rapidly improved. No further red blood cell transfusions were required. In October 2007, the patient's hemoglobin level was within the normal range, and the PVB19-DNA load decreased to 10^{5} copies/ml. Although reexamination of bone marrow aspirate was not performed, PVB19-induced PRCA was completely resolved, and PVB19 IgG antibody was persistently detected; PVB19-DNA (10^{3} copies/ml), however, was still detected.

Discussion

IRIS is a serious condition that can occur after the initiation of HAART. This syndrome is usually self-limited, but it may worsen and necessitate intervention. In our case, the patient presented with transient inflammatory responses, such as fever, shortly before the remission of PRCA. The laboratory results revealed leucopenia, atypical lymphocytes, and elevation of the serum LDH level; these findings were similar to those of a nonspecific response to viral infections. Additionally, his anemia rapidly worsened despite showing some improvement shortly before this episode. His immunological state was improving: the CD4 cell count rose, seroconversion to anti-PVB19 IgG antibody was observed, and the serum PVB19-DNA level showed a slight but significant decrease. On the basis of these paradoxical findings, we thought that this was an episode of IRIS. The recent literature contains only two reports of severe IRIS. In one of the cases, the patient presented with acute encephalitis [10]. In that case, the patient had persistent PVB19 infection, and the complication of chronic PRCA was treated with intravenous Ig therapy. Four weeks after initiating HAART, anemia developed rapidly with acute onset of ataxia and aphasia. Such a progression was unexpected because encephalitis is a rare complication in PVB19 infection. In the other case, acute and transient anemia developed after the initiation of HAART, although no anemia and PVB19 infection were detected before HAART [11]. Serum antibodies to PVB19 had not been fully confirmed in either of these cases. In all three cases, rapid deterioration of anemia was observed after HAART; this finding seems to be a typical presentation in IRIS associated with HAART for PVB19 infection. With the exception of anemia, the symptoms and pathogenic conditions observed in our case are different from those observed in the two above-mentioned cases. Our case seems to be the most typical presentation of IRIS because (1) the patient was proven to have a chronic PVB19 infection before HAART, (2) the immunological parameters, such as the CD4 cell count and IgG antibody production, showed an improvement during the course of IRIS, and (3) the patient developed symptoms resembling those of acute viral infection. The diagnosis of PVB19-associated IRIS with atypical features may be difficult because of the lack of diagnostic criteria. However, the

findings in our case suggested that seroconversion to antibody against PVB19 and the presence of anemia are helpful in diagnosing PVB19-related IRIS.

The production of neutralizing antibodies plays a pivotal role in the immune control of PVB19 infection [3]. Specific IgM and IgG antibodies are produced 2 and 3 weeks, respectively, after primary PVB19 infection, and these antibodies are responsible for the elimination of PVB19. The EIA kits used in this case could be used only for qualitative assessments. However, the EIA indices of anti-PVB19 IgG and IgM antibodies can indicate the titer of antibodies because these EIA kits include strong positive controls with EIA indices that are at least higher than 1.5, and the EIA indices of the clinical samples were up to 15 and showed good reproducibility. When evaluated on the basis of EIA indices, the anti-PVB19 IgM antibody level showed moderate elevation during primary PVB19 infection. In contrast, the samples were weakly negative for the anti-PVB19 IgG antibodies. These observations suggested that the class-switch recombination of B lymphocytes was markedly disturbed during the infection, and this was probably because of the dysfunction of $CD4^+$ T lymphocytes. Lack of these protective antibodies may lead to the transition from primary to persistent infection and permit high-level PVB19 viremia [12].

In the pre-HAART era, some cases of chronic PRCA with persistent PVB19 infection were treated with intravenous Ig therapy [5], in which the patients were administered neutralizing antibodies to PVB19. This treatment results in a rapid decrease in the copy number of blood PVB19-DNA from 10^{10} to 10^6 copies/ml and improvement of anemia [13]. However, this treatment has a transient effect, and many patients show recurrence of PRCA after the treatment. It should be noted that this therapy cannot clear the PVB19-DNA in the blood, and the DNA persists at levels of about 10^6 copies/ml. These observations suggest that administration of neutralizing antibody alone is insufficient for eliminating PVB19. In our case, the patient developed chronic PRCA, and the serum PVB19-DNA level was 10^{10} copies/ml. Even after seroconversion to anti-PVB19-DNA IgG antibody and the resolution of PRCA, the viremia persisted, and the patient had viral loads of 10^3–10^5 copies/ml. We cannot exclude the possibility that this might be caused by the production of an incomplete neutralizing antibody [7]. PVB19 was, however, not eliminated in our patient, as was also the case in previous reports of treatment with intravenous Ig. This indicates the importance of immune mechanisms other than humoral immune responses [14], such as those involving cytotoxic T lymphocytes.

In our case, the relationship among clinical observations, immunoserological findings and the serum viral load could be evaluated because intravenous Ig was not administered and immune recovery was prolonged. Physicians must note that PVB19 can cause severe anemia in HIV-1-infected patients [14], and detection of PVB19-DNA must be performed in immunosuppressed patients because of the lack of specific antibodies [12]. In addition, detailed investigations on immune reactions to PVB19 will facilitate a better understanding of the mechanism underlying immune reconstitution by HAART.

Written informed consent was obtained from the patient for publication of this case report. A copy of the written consent is available for review from the journal's Editor-in-Chief.

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Conflict of interest The authors have no conflicts of interest to declare.

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特集

麻酔前の評価・準備と予後予測 I

緒言とまとめ

澄川　耕二

麻　　酔
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論　説

最近のプレホスピタルケアについて考える

平成3年救急救命士法が成立し，救急救命士は心肺停止患者に対する除細動，血管確保と輸液の3点セットが，医師の指示のもとに行われるようになった。当初は心電図を医師のもとに伝送して心室細動を確認し，救命士が行うという，とても時間がかかって有効とは思えないことが，時代の流れで行われてきた。その後，早期除細動の有効性が徐々に啓蒙され，救命士は包括的指示のもとに除細動が行えるようになった。そして，平成17年，現場での除細動が市民によっても可能となった。その年からウツタイン様式（心肺停止患者の検証）が全国一斉に総務省が中心になって行われ始めた。その結果を見ると，目撃のある心原性の心停止患者の1カ月生存率，1カ月後社会復帰率はそれぞれ（7.2-3.3%：2005年，10.4-6.6%：2008年）と上昇してきている。これには救命処置の講習会やBLS，ACLSなどのコースが全国展開され，救命に対する関心が社会的に高まってきたことと，一般市民もAEDを使用できること，AEDがあたかも消火器が普及するかのごとく至る所に設置されるようになったことが寄与していると考えられる。現在では，贈答品にもAEDが使用されるに至っている。

一方，救急救命士法が施行される前，プレホスピタルにおける救急隊員が行う気管挿管について議論が沸いた。私の師匠，故・奥秋　晟 福島県立医科大学名誉教授は，救急隊員による気管挿管には批判的であった（麻酔第38巻9号巻頭言）。救急現場には医師が行くべきであり，気管挿管も含めた救急処置は医師がするべきであるという立場をとっていた。気管挿管の技術の習得と適応の判断の難しさを指摘されていた。また，気管挿管よりも用手的気道確保こそ大切であること，そして，誤挿管などの合併症があった場合，責任の所在を救急隊員に求めるのは酷であることなどが主な理由であり，“私は救急隊員を守りたい”と話していた。救命士が誕生して，平成14年に秋田県と山形県の救急救命士による気管挿管という違法行為が発覚し，プレホスピタルでの気管挿管に関しての議論が再発した。世論を背景に総務省の指導のもと，救命士による気管挿管が可能となった。麻酔科学会もこれを支持する立場をとり，現在，各病院の麻酔科医は気管挿管に関する授業や病院手術室での気管挿管実習成功例30症例に寄与している。

しかしながら，2000年そして2005年AHA心肺停止に関するガイドラインにおいて，気管挿管の有効性に関するエビデンスは低下してしまった。むしろ心マッサージ，つまり胸骨圧迫を早く，強く，確実に，絶え間なく行うことこそ重要で，気管挿管に時間を要して，胸骨圧迫が中断されてはならないとさえいわれている。

一方，気管挿管許可者となった救命士の気管挿管施行回数をみると，地域によってかなりの差があるが，1名あたり年に1-2症例である。10症例以上の挿管経験者はきわめて少ない。経験がないので，3年おきに病院実習，または講習会などで再教育しているのが実情である。救急現場での気管挿管は，手術室のように準備万端整えられ安全確実に行われるとはかぎらない。心停止状態なので不動化となっており，容易に行えると考えている医師は少なくないが，決して簡単ではない。エビデンスが低く気管挿管を経験する機会も少ないとなると，救命士のモチベーションは低下するばかりである。また，患者からインフォームドコンセントを取り，気道確保の手技を教授し，気管挿管の指導を担当している麻酔科医の意欲も消えてなくなる可能性がある。

心原性患者に対する気管挿管の救命率が高くないのは，適応がない患者にも気管挿管が行われている例もあり，そのために予後の改善という結果に至らない可能性は否定できない。最近のウツタイン様式の結果では，非心原性患者への気管挿管に関しては救命率が高そうだという報告があるが，患者背景が明白ではなく結論は出ていない。

気管挿管も含めて，麻酔科学会としての考え方も再検討する時期に入ったのではないかと思う今日このごろである。

（山形大学教授　川前　金幸）

麻酔 2010；59：817.

特集

麻酔前の評価・準備と予後予測 I

緒言とまとめ

澄川　耕二

キーワード 術前診察，麻酔前評価，麻酔前準備，予後予測，術後合併症

手術を受ける患者の麻酔にあたっては，周術期管理の質を高め，合併症を減少させ，できるだけ早く日常生活に戻すことが求められる。それを実現するうえで肝要なことは，患者のリスクを把握し，対策を準備し，有効な周術期管理を実施することである。これに伴って予後を予測し，インフォームドコンセントを得ることも必要である。本特集では術前診察において特に重要なポイントを最新のデータに基づいて解説する。

呼吸器疾患については篠崎，福岡，飯田らが解説する。気管支喘息の重症度評価は症状の特徴に呼吸機能検査の1秒量とピークフローを加えて行う。術前治療では重症度に応じて，ステロイド薬の吸入，内服，点滴静注の適応を選択する。成人喘息の28%でアスピリンおよび非ステロイド性抗炎症薬（NSAIDs）の使用で急性増悪が見られるため，周術期には特に注意を要する。

慢性閉塞性肺疾患（chronic obstructive pulmonary disease：COPD）はタバコ煙を主とする有害物質の長期曝露により生じる。喫煙患者の15%はCOPDを伴う。安定期における血液ガス分析値は手術に伴う死亡リスクを予測する。高二酸化炭素血症を呈する患者の院内死亡率は約10%とされる。術後呼吸器合併症は正常者の3-4倍リスクが高い。特に上腹部・胸部手術，3時間を超える手術で頻度が高く，術前の呼吸訓練が勧められる。肺炎の頻度は正常者の1.5%に対し，COPD患者では3.5%である。

特発性間質性肺炎を有する患者では術後呼吸器合併症のリスクが高く，肺癌手術の予後不良因子である。周術期における急性増悪は約40%と高率で，急性増悪を来した場合は致死的である。高濃度酸素投与は急性増悪の誘因となる可能性がある。Pa_{O_2}を80-100 mmHgに保つよう吸入酸素濃度を下げるのが好ましい。

喫煙患者では周術期呼吸器合併症が増加する。酸素運搬能低下と免疫抑制から創部の離解や感染が増える。冠動脈バイパス術患者の術後呼吸器合併症の頻度は，術前8週間以内の禁煙では効果なく，12週間以上で有意の改善が見られる。

心血管疾患については原，河野，恵川，井上らが解説する。心疾患患者では日常生活における活動量が4 METs（掃除や皿洗いなどの簡単な家事）に満たない場合，周術期の心リスクが増加する。非心臓手術の前に冠血行再建術が勧められる症例は，左冠動脈主幹部病変，三枝病変，不安定狭心症，心筋梗塞などである。冠動脈ステント留置後の抗血小板療法はbare-metalステントで4-6週間，drug-elutingステントで12カ月継続しなければならない。この間，待機的手術は延期する。

低心機能の重症度評価に左室駆出率が重要である。慢性心不全では駆出率25%未満は年間死亡率が急上昇し，20%未満では半年内死亡率が70%に上る。低心機能患者の重度危険因子は，非代償性心不全，重度の不整脈，重度の弁膜症であり，緊

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急手術でなければその治療を優先する。重症の大動脈弁狭窄症では非心臓手術の周術期死亡率が10%に上るため，一般に，非心臓手術の前に弁置換術を行う。

不整脈のうち手術を延期すべき重度危険因子は，Ⅲ度房室ブロック，モビッツⅡ型房室ブロック，症状のある心室頻拍，安静時心拍数 100 beats・min^{-1}以上の心房細動，症状のある徐脈，などである。ペースメーカ装着患者では，さまざまな電磁干渉により，ペースメーカの誤作動，不適切な刺激抑制，機器の故障といった不具合を生じる可能性があり，術前に対策を講じる必要がある。また，予期せぬペースメーカ不全に備えて，陽性変時作動薬，緊急ペーシング，除細動器などを準備しておく。

脳梗塞急性期には梗塞部位の組織が脆弱化しており，出血や虚血の増悪を来しやすく，発症から1カ月は手術延期が望ましい。くも膜下出血全体の死亡率は10-67%で，予後と相関するものは発症時の意識障害の程度である。くも膜下出血は交感神経過緊張を伴い，狭心症，心筋症などの循環系障害を起こす可能性があり，12誘導心電図の評価は特に重要である。心拍出量低下症例では，たこつぼ型心筋症も考慮に入れ，心エコー検査を行う。

深部静脈血栓症の重症度診断には下肢静脈エコーが有用である。画像から，陳旧性か新鮮性か，遠位部か近位部かを診断する。新鮮性で近位部のものが肺血栓塞栓症を発症しやすい。深部静脈血栓症が診断されるとその時点から抗凝固療法の対象となる。術前であればヘパリンの持続投与を開始する。肺血栓塞栓症のリスクの高い症例では抗凝固療法に加えて一時的下大静脈フィルタの留置を考慮する。

代謝・内分泌疾患については竹田，正宗らが解説する。糖尿病患者は老化が早く，暦年齢1歳に対し血糖コントロール良好では1.06歳，不良では1.5歳年をとる。これに伴いさまざまな臓器障害を合併する。心筋梗塞の発症頻度は非糖尿病患者の2倍で，高血圧が加わると8倍，さらに高脂血症が加わると19倍となる。術後合併症の2/3を感染性合併症が占め，死亡率の20%が感染による。

肥満患者の術前合併症の頻度は，脂肪肝100%，睡眠時無呼吸82%，高血圧68%，糖尿病59%，胃食道逆流症36%，うつ36%，気管支喘息25%，冠動脈疾患18%とされる。術前評価にあたっては，気管挿管困難，睡眠時無呼吸，肥満性低換気症候群，心機能，深部静脈血栓症などの評価が特に重要である。

甲状腺機能のコントロールが不良の場合，甲状腺クリーゼや粘液水腫になると非常に致死率が高いので，術前に甲状腺機能を正常にすることが重要である。褐色細胞腫の麻酔管理に際しては，α遮断薬による術前治療がしっかりなされることがもっとも重要であり，これにより，循環動態の安定化とともに，循環血液量の回復とカテコラミン誘発性心筋炎の改善が期待できる。

肝・腎疾患については箱崎，飯田らが解説する。急性肝炎で試験開腹手術を受けた患者の周術期死亡率は10-30%と高い。したがって，肝細胞障害が改善するまで予定手術は延期する。肝硬変患者の開腹手術における死亡率はChild-Turcotte-Pugh分類のA，B，Cでそれぞれ，10%，30%，82%とされている。慢性腎不全の重症度はクレアチニンクリアランス値による病期分類で判定し，周術期管理に反映させる。心臓手術では術前腎機能が悪いほど術後院内死亡が増加する。血清クレアチニン1.4-2.2 mg・ml^{-1}の中等度腎障害も周術期死亡率，術後人工透析，心房細動発生率を増加させる。

ABSTRACT

Preoperative Evaluation, Preparation and Outcome Prediction：Preface and Comments

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In the practice of anesthesia for the patients undergoing surgery, it is required for anesthesiologists to improve the quality of perioperative management,

decrease adverse events, and help the patients return to daily life as soon as possible. The conditions crucial in realizing this purpose include risk assessment, preparation of measures and implementation of effective perioperative management. Furthermore, it is also necessary to obtain informed consent based on reliable outcome prediction. In this special issue, essential points for preoperative evaluation will be presented on the basis of up-to-date information.

key words：preoperative evaluation, risk assessment, outcome prediction

特集

麻酔前の評価・準備と予後予測 II

緒言とまとめ

澄川　耕二

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論　説

専門医制度

麻酔科は，わが国の臨床診療科の中において比較的新しく構築された診療科であり，その歴史は60年ほどにしかならない。が，その中にあって日本麻酔科学会がすべての診療科に先駆けて昭和37年に専門医（麻酔指導医）制度を発足させたことは有名であり，麻酔科学会の先人達の慧眼には深く敬服させられる。その後，専門医制度の確立が各分野で議論された結果，昭和56年に22学会が集まって学会認定医制協議会の第1回総会が開催された。平成5年にこの学会認定制協議会と日本医師会，日本医学会の三者懇談会で14の基本領域が設定（現在18学会に増加）された。平成13年に，学会認定制協議会は，専門医認定協議会となり，その翌年に中間法人日本専門医制認定機構，さらに平成20年に社団法人日本専門医制評価・認定機構へと改組された。現在機構に所属する学会は，この基本領域18学会以外にsubspecialtyの学会（専門医取得に特定の基本領域の取得が必須な学会）として消化器外科学会など26学会，多領域に横断的に関連する学会として集中治療医学会など7学会，その他新規加入学会などいまだ分類されていない学会（ペインクリニック学会など）などを含めて，全部で75学会を数える。ちなみに，心臓血管麻酔学会は現時点で未加盟である。専門医を機構自体が認定するのではなく，従来の学会が独自に認定するという枠組みは残しつつ，制度が不統一で必ずしも質が担保されていない点を改善することが機構の一つの役割とされている。

この間，平成14年に厚生労働省の規制緩和によって専門医表示が自由化された。診療科の標榜はいまだ規制が強いなかで，専門医表示は比較的緩やかという，ややいびつな構造ができあがったともいえる。ペインクリニック専門医は表示できても，ペインクリニック科という表示は違法ということである。専門医表示については日本医師会，日本医学会，認定機構の三者による認定と承認が好ましいと筆者も考えるが，厚労省は制度を早く発足させるために“学会の定める専門医制度が外形基準を満たしてさえいれば専門を自由に表示できる”としたところに問題があるのかもしれない。ただ，そうでもしなければなかなか問題が先に進まなかったことも事実ではある。いずれにしろ，この専門医表示の問題は今後，診療科表示との絡みでどのように改善されていくのか注目しなければならない。

著者自身のことで申し訳ないが，これまで専門医資格として麻酔科指導医（専門医），集中治療専門医，そしてペインクリニック専門医を取得している。いずれも15年以上にわたって更新を続けつつ維持してきた。麻酔科専門医は基本領域で，後の2つはその他ということになる。ところが近年，機構の指導もあり専門医の更新手続きはどんどん変化し，場合によっては敷居が高くなってきている。私自身も，近年ペインクリニック専門医の更新手続きが大きく変わったことにより，外来での必要症例数などの更新基準をクリアすることはまったく困難となった。今回はとりあえず猶予申請したが，このままでは確実に専門医資格を喪失することになろう。このような事情は集中治療専門医資格についても同様である。そのため，集中治療医学会では現在，制度改革のための専門医制度検討委員会で議論がなされている。著者もその委員の一人であるが，既得権利を有する医師の種々多様な希望にも応えるべく，さまざまな提案が委員会内外から出されようやく方向性が見いだせるところまでに至った。一番問題となったのは，やはりペインクリニックや集中治療という分野は麻酔科という母体教室があって初めて成り立つという形が，一部の例外施設を除けば，多くの大学や病院で一般的であるという点であった。すなわち，近年の手術麻酔の増加のため個人の希望などとは別に教室の都合もあって手術麻酔専従に帰り，今後求められる症例数などをクリアできずせっかく取得した専門医資格を泣く泣く手放さねばならなくなる医師が少なからず現れるだろうということである。集中治療医学会の専門医制度検討委員会ではこの点を問題視し，すでに集中治療専門医を取得してその後に資格喪失した人々にも，比較的敷居の低い条件で再度専門医資格を与えるという案を練りつつある。細部は決定していないので，今後の動向を注目していただきたいが，個人的にはペインクリニック学会にも同様の動きがあることを期待する。

いずれにしろ専門医資格を取得したときに，どのようなインセンティブがあるかこの点を十分念頭におき，たとえば専門医がいれば施設基準をクリアして加算可能となるといった働きかけを厚労省へ働きかけるという姿勢も各学会には必要であろう。欧米先進諸国では，このような専門医資格はすべて定数制である。わが国だけが医師に選択権があり，その資格取得が比較的簡単であったという点にも改革の余地があると考える。

現在の案において問題になるであろうと考えられるもう一つの問題点は，救急専門医が基本領域に位置づけられている点である。ご存じのように，わが国の多くの救急専門施設は外科，内科，麻酔科，整形外科，脳神経外科などの医師で構成されている。すでに述べた平成5年の三者懇談会では，基本領域の設定と同時に，この基本領域の専門医を2つ以上持つことを禁止することで合意している。この合意が現在も継続していることはさほど知られていない。すなわち，普通に考えれば，救急専門医は麻酔科専門医や外科専門医を同時に保有することができないことになる。やはりわが国の現状を鑑みて，例外事項として救急専門医に関しては複数の専門医資格の保有を認めるべきでないかと筆者は考える。以上問題点の羅列となってしまい，具体的解決案には乏しいものとなったが，ぜひ読者の皆様もこの機会に専門医とは何かという問題を問うてみていただきたい。

（京都府立医科大学集中治療部教授　橋本　　悟）

麻酔 2010；59：1085.

特集

麻酔前の評価・準備と予後予測 II

緒言とまとめ

澄川　耕二

キーワード 術前診察，麻酔前評価，麻酔前準備，予後予測，術後合併症

神経・筋疾患については，山内，須藤，木村らが解説する。重症筋無力症に対して拡大胸腺摘除術が施行された場合，術後合併症は 33％に発生し，クリーゼに伴う急性呼吸不全（6％），感染症（11％），反回神経・横隔膜神経損傷（2％）などがある。死亡率は 1％以下である。5 年寛解率は非胸腺腫症例において 45.8％，胸腺腫症例では 23.0％である。

筋ジストロフィの術前評価では，病歴，呼吸機能障害，心伝導障害，心筋症，筋拘縮，脊椎変形，胃内容物の停滞などが問題となる。特に，呼吸筋力の低下，胃内容物の停滞は術後呼吸管理や誤嚥と肺炎の危険性が増す。高度房室ブロックを有すれば，心ペースメーカの必要性を考慮する。周術期の重篤な合併症としては，悪性高熱様反応，黄紋筋融解症，それに伴う高カリウム血症による心停止などがある。

てんかん患者の麻酔管理で，発作以外に問題となるのは抗痙攣薬の副作用である。抗痙攣薬は肝機能障害，腎機能障害，貧血，白血球減少などを来す場合があり，術前の検査で各項目を確認しておく。また，副作用により歯肉増殖を起こし，気道確保に難渋した報告もあり，口腔内を確認しておくとよい。

多発性硬化症の麻酔に関しては，脊髄くも膜下麻酔や硬膜外麻酔が症状を増悪させるという報告が多い。脱髄した神経が，局所麻酔の神経毒性を受けやすくなると考えられているためである。近年の報告では，麻酔方法の選択と症状増悪との因果関係はないとするものもあるが，全身麻酔よりも脊髄くも膜下麻酔や硬膜外麻酔のほうが有利であると考えられるとき以外は，避けるべきであろう。

精神疾患については工藤が解説する。統合失調症患者では突然死が多いことが知られているが，“phenothiazine death”で表されるようにフェノチアジン系抗精神病薬は明らかに統合失調症患者の突然死に関与している。定型抗精神病薬は，特に QT 延長症候群や多型性心室性頻拍に注意しなければならない薬物とされている。

うつ病自体が虚血性心疾患や急性心筋梗塞の危険因子となる。心筋梗塞で死亡する割合は約 4 倍高い。さらに，三環系抗うつ薬は心血管系疾患の危険因子と考えられており，心筋梗塞になる割合は 2.2 倍高い。四環系は三環系に比べて心臓に与える影響は少ない。一方，SSRI はむしろ心血管疾患に対し予防的効果を有すると報告されている。

特殊素因については仁科，植木，右田，河本，森山，萬らが解説する。近年，胎児期や乳幼児期に全身麻酔を受けることにより脳発育に悪影響をもたらす可能性が示されている。しかし，脳発育への影響はどの程度の影響が，どの程度の期間残り，回復可能なものか麻酔自体が悪影響を引き起こしているのか，入院や手術などすべての環境因子が複合的に影響を与えた結果なのかはまだ明ら

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かになっていない。

65 歳以上の高齢者の手術リスクと予後は，主に年齢，患者の生理学的状態および合併症，待機手術か緊急手術か，手術の内容の 4 つの因子に依存している。以前の研究から合併症は年齢により増加するとされ，Goldman の心臓リスク・インデックスでは，70 歳以上は独立した高度危険因子として扱われている。

悪性高熱症素因患者では麻酔法の選択が重要である。すべての揮発性吸入麻酔薬や脱分極性筋弛緩薬は，悪性高熱症を誘発しうる。静脈麻酔薬や麻薬性鎮痛薬，非脱分極性筋弛緩薬は誘発しない。したがって，素因患者でも全静脈麻酔などで安全に麻酔管理が可能である。局所麻酔薬も安全であり，脊髄くも膜下麻酔や硬膜外麻酔も実施可能である。

挿管困難の予測には，開口の程度，Mallampati 分類，頭頸部の可動性（環椎後頭関節の可動性），下顎の後退，上顎切歯の前突，甲状頤間距離，胸骨頤間距離，upper lip bite test，肥満，挿管困難の既往など多要因が関係するため，単一の因子での予測は困難である。しかし，現時点で評価の高いのは，Mallampati 分類と甲状頤間距離である。

感染症に対する対策として，米国疾病管理予防センター（Centers for Disease Control and Prevention：CDC）は標準予防策と感染経路別予防策よりなる“隔離予防策のための CDC ガイドライン”を発表した。標準予防策は，手指衛生，手袋，ガウン，マスク，眼防御，安全な注射手技などからなる。血管穿刺では手袋のみ，気管挿管では手袋＋ガウン＋フェイスシールドが必要となる。2007 年の改訂で，呼吸器衛生/咳エチケット，安全/清潔な注射手技，腰椎穿刺および硬膜外へカテーテル挿入時のマスク装着が加えられた。感染経路別予防策は，標準予防策のみを実施しても感染経路を完全には遮断できない場合に用いる。

エホバの証人への対応として，幼児などで明らかに判断能力がない場合に問題が多い。患者にとって無輸血が不利益であると医療者が判断すれば，法的措置に訴えるまでもなく，親権者の代行判断を無視しても違法ではないとの見解がある。判断能力がない 15 歳未満の患者には，相対的無輸血の方針が無難である。

術前常用薬については葛川，山本らが解説する。降圧薬のうち，アンギオテンシンⅡ受容体拮抗薬（ARB）の投与を受けている患者では，手術当日まで ARB を継続すると全身麻酔導入後の重篤な血圧低下が起こることが示されている。よって，ARB は手術前日までで中止するほうがよい。

ステロイド薬に関しては，周術期においてもしもストレスがなければ，副腎皮質ホルモンが欠乏している患者でも一般的に問題はない。しかし，軽度でもストレスがある場合には急性副腎不全が起こる可能性がある。成人で 25 mg のリン酸ヒドロコルチゾンを手術開始時に経静脈的に投与し，引き続く 24 時間で 100 mg を静脈内投与する。この方法では最大量 300 mg を使用した方法と同程度に有効であることが分かっている。

抗凝固薬や抗血小板薬使用患者に脊髄くも膜下麻酔や硬膜外麻酔を行う際の休薬期間については，2003 年に公表された米国局所麻酔学会のガイドラインが広く受け入れられている。ワルファリンは 4-5 日前から休薬し，脊髄くも膜下麻酔や硬膜外麻酔を行う前に PT-INR が正常範囲内であることを確認すること，カテーテル抜去時にも PT-INR が 1.5 未満であることを確認することが勧められている。アスピリンの単独投与（75-300 mg・day^{-1}）が脊髄くも膜下麻酔や硬膜外麻酔による硬膜外血腫の発生頻度を増すという報告はないため，休薬の必要はないとされている。抗血小板薬のチクロピジン塩酸塩は 14 日前から，硫酸クロピドグレルは 7 日前からの休薬が推奨されている。

避妊薬あるいは子宮内膜症治療薬として投与される低用量ピルは，深部静脈血栓症をはじめとする静脈血栓塞栓症の発生を増加させるが，絶対危険度は高くはない。国内の経口避妊薬添付文書には，“術前 4 週以内と術後 2 週以内の低用量ピルの使用は禁忌”と記載されており，周術期には低用量ピルの使用を中止するのが妥当であろう。

ABSTRACT

Preoperative Evaluation, Preparation and Outcome Prediction Ⅱ：Preface and Comments

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In this special issue, essential points in preoperative evaluation are presented on the basis of up-to-date information. Myasthenia gravis should be evaluated according to individual severity. Muscular dystrophies may lead to rhabdomyolysis perioperatively. Schizophrenia is predisposed to developing torsade de pointes. Depression could be a risk factor of acute myocardial infarction. Infants may be influenced by anesthesia with respect to brain development. Elderly patients should be evaluated on the basis of age, physiological states, coexisting diseases and the type of surgery. Difficult airway management can be predicted by Mallanpati classification and thyromental distance. Jehovah's Witness of ages below 15 should be informed about the policy of life-saving blood transfusion. Oral contraceptive is associated with a fivefold-increased risk of perioperative venous thromboembolism.

key words : preoperative evaluation, neuromuscular disease, disposition, preoperative drug

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ORIGINAL RESEARCH

Effects of Nitric Oxide Donor on Hepatic Arterial Buffer Response in Anesthetized Pigs

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ABSTRACT

The effects of systemic administration of exogenous nitric oxide (NO) donor on hepatic arterial buffer response (HABR) have not yet been studied in an anesthetized model. In this study, 28 anesthetized pigs received administration of sodium nitroprusside (SNP) or nitroglycerin (NTG) as exogenous NO donors. Pressure-flow (P-Q) relationships in the hepatic artery defined the pressure at zero flow ($P_{Qha=0}$) and flow-dependent resistance (R). The magnitude of HABR was evaluated by comparing the change in hepatic arterial blood flow (ΔQha) divided by the change in portal venous blood flow (ΔQpv), using the index of change in blood flow (ΔQha/ΔQpv). Mean arterial pressure decreased from baseline (95.6 ± 3.8 mmHg) to SNP condition (68.3 ± 1.9 mmHg) and decreased from baseline (92.7 ± 4.4 mmHg) to NTG condition (66.2 ± 1.7 mmHg). Mean index of change in blood flow (ΔQha/ΔQpv) was also significantly increased from baseline (0.19 ± 0.12) to SNP condition (0.28 ± 0.17; $p = .009$) and from baseline (0.18 ± 0.17) to NTG (0.28 ± 0.20; $p < .05$). In conclusion, systemic administration of SNP and NTG increases HABR with reduced hepatic arterial tone under decreased mean arterial pressure, presumably via exogenous NO enhancing another regulatory system and reducing the pressure gradient for sinusoidal washout.

Keywords: hepatic arterial buffer response, pig, nitric oxide, sodium nitroprusside (SNP), nitroglycerin (NTG)

INTRODUCTION

Total liver blood flow is regulated by changes in hepatic arterial resistance (Rha), when portal venous blood flow (Qpv) changes as the hepatic arterial buffer response (HABR). A number of studies have revealed modification of HABR function under pathophysiological conditions, including both the maintenance of HABR under hypotension conditions [1–3] and the impairment of HABR [4–6].

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Endogenous nitric oxide (NO) represents an important regulator of hepatic arterial flow [2, 6–10]. However, it has also been suggested that endogenous NO does not mediate the HABR under physiological conditions [6, 9]. We have previously found that under anesthesia, local control of hepatic arterial blood flow (Qha) at baseline showed increased gain after NO-synthase (NOS) inhibition, via HABR and autoregulation [6]. Furthermore, Grund et al. [9] reported that NO represents an important regulator of Rha but does not mediate the HABR. Since NO normally diminishes autoregulatory control in other organs, inhibition of NOS in the hepatic artery indeed could be expected to increase gain in the HABR.

Sodium nitroprusside (SNP) and nitroglycerin (NTG) are nonenzymatic NO donors that have commonly been used as vasodilators to control arterial pressure during general anesthesia. Although the influences of SNP and NTG on systemic circulation and splanchnic circulation have been extensively studied [1–4], little information is available regarding the effects of SNP and NTG on HABR under inhalational anesthesia. We hypothesize that systemic administration of SNP and NTG significantly influences HABR in different ways. The purpose of the present study was to investigate the quantitative influence of systemic administration of exogenous SNP and NTG on HABR in a physiological anesthetized porcine model established previously [6, 11, 12].

MATERIAL AND METHODS

The study protocol was approved by the animal research committee of the Nagasaki University and complied with the animal research and animal care guideline of the Japanese Ministry of education, Science, Sports and Culture.

Twenty-eight male pigs with a body weight of 21–27 kg (mean 24.8 ± 4.2 kg) were fasted for 24 hr with ad libitum access to water. As described in our prior study [12], anesthesia was induced using intramuscular administration of pentobarbital sodium (10 $mg \cdot kg^{-1}$) and ketamine (20 $mg \cdot kg^{-1}$) followed by cannulation of an ear vein and intravenous (i.v.) administration of additional pentobarbital sodium (2 $mg \cdot kg^{-1}$). All surgical procedures were performed under sterile conditions. Since the whole study was maintained sterile at all times and lasted such for a short time (approximately 3 hr) with no survival included, we did not use antibiotics as pre-emptive antiseptic therapy in this study. Pigs were placed in a supine position on a heated surface (38–40°C), and tracheotomy was performed. Anesthesia was maintained with sevoflurane 2% plus 50% nitrous oxide and 50% oxygen in order to obtain adequate analgesic effect while continuously measuring the expired gas concentration of sevoflurane (Narcotica; Fukuda Denshi, Tokyo, Japan). As muscular relaxation was needed for surgical instrumentation and measurement of pressure-flow relationships without any respiratory fluctuations, neuromuscular blockade was maintained using a nondepolarizing agent (vecuronium bromide) administered with the evidence of spontaneous muscle activity. Mechanical ventilatory support was provided using a constant volume time-cycled ventilator. Tidal volume (8–12 $ml \cdot kg^{-1}$) and ventilatory rate (12–14 $cycles \cdot min^{-1}$) were adjusted to maintain arterial partial pressure of carbon dioxide (PCO_2) within 30–40 torr.

The right carotid artery was cannulated with a fluid-filled catheter for the measurement of systemic mean arterial pressure (mean $Psys_{art}$) and withdrawal of blood samples. The right subclavian vein was cannulated for fluid infusion and drug administration. A balloon-tipped pulmonary arterial catheter was inserted via the right internal jugular vein to measure cardiac output.

The liver was exposed by a midline abdominal incision. A drainage catheter was inserted into the urinary bladder. The portal vein and common hepatic artery were gently dissected free from surrounding tissue. A fluid-filled catheter was inserted into the portal vein through the side branch to 1 cm of the hilum of the liver to measure portal venous pressure (Ppv). The gastroduodenal artery was cannulated with a fluid-filled catheter to measure hepatic arterial pressure. Care was taken that the catheter tip was positioned at the bifurcation of common hepatic and gastroduodenal arteries to optimize the pressure recording without obstructing flow to the liver. The right gastric artery, cystic artery, and all other hepatic arterial branches were ligated so that the common hepatic artery was the only artery supplying blood directly to the liver. We used splenetomized animal model, in which all other tributaries of the portal vein between the splenic vein and liver hilum were ligated in order to establish the theoretical maximal increase of Qha in response to a reduction of Qpv. After this general surgical preparation was completed, splenectomy was performed so that Qpv was exclusively supplied by the superior mesenteric artery. All branches of the celiac artery were ligated (right gastric artery, splenic artery, and all other collaterals) so that the hepatic artery was exclusively supplied by the celiac artery. Hydraulic vessel occluders (inner diameter 6 mm; outer diameter 12 mm; length 8 mm; Hazen Everett, NJ, USA) were placed around the celiac artery and superior mesenteric artery to allow independent control of both flows. Appropriately sized ultrasonic flow probes were placed downstream around the common hepatic artery and portal vein.

A catheter was placed in the anterior hepatic vein via the external jugular vein, and location of the catheter was confirmed by direct palpation. The catheter was withdrawn 0.5–1.0 cm from the wedge position to allow measurement of hepatic venous pressure. When surgical procedures were completed, the abdominal wall was reapproximated and towels were placed on the surface to minimize heat loss.

Methods of Measurement

Blood flows were measured using ultrasound transit time flow probes (Transonic, Ithaca, NY), and vascu-

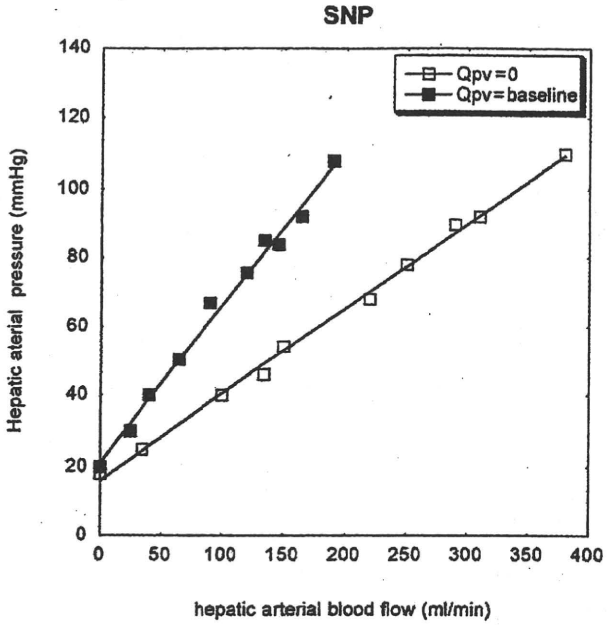

Figure 1. Experimental protocol. Pressure-flow (P-QR) relationships were generated at baseline and under SNP and NTG infusion.

lar pressures were measured with pressure transducers (AP-611G; Nihon Kohden, Tokyo, Japan). Pressure and flow signals were continuously recorded on a pen recorder (WR8500–8; Nihon Kohden). Pressure transducers were calibrated simultaneously with the same gain and zeroed to the level of the portal vein. Cardiac output was measured at the beginning of each condition with baseline Qpv and Qha using a thermodilution computer (AP-611G; Nihon Kohden). Five serial injections of 5 ml of ice-cold 5% dextrose solution were made at arbitrary times within the respiratory cycle, and the five values of cardiac output were averaged. Arterial blood gas measurements were made using an I-STAT analyzer (FUSO, Tokyo, Japan).

Pressure-flow (P-Q) Relationships

Hepatic arterial pressure-flow (P-Q) relationships were generated during multiple-step decreases in Qha from baseline to zero produced by gradual inflation of the occluder on the celiac artery. The following criteria were used to generate a P-Q relationship in the hepatic artery under steady-state conditions. A wide flow range from 0 to 100% of hepatic artery baseline flow was used, and zero-flow pressure ($P_{Qha=0}$) was obtained at actual zero flow. Stable flow and pressure (15–30 s following a step decrease in hepatic artery flow) were required with constant P_{hv}. Hepatic arterial P-Q relationships were analyzed using least-squares linear regression analysis to determine the slope and zero flow pressure axis intercept in the hepatic artery ($P_{Qha=0}$)

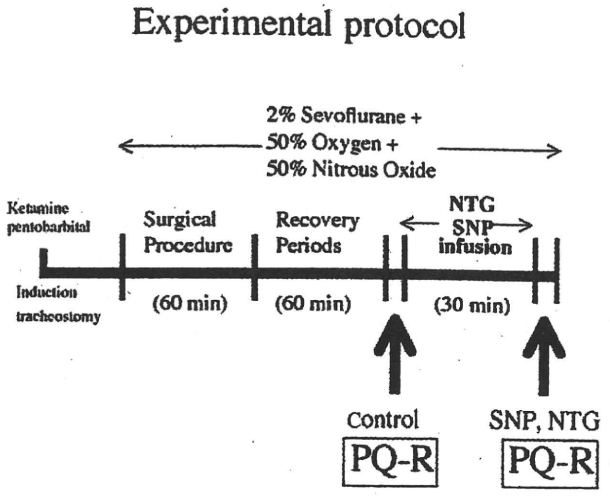

Figure 2. Example of hepatic arterial pressure-flow (P-QR) relationships. There was significant ($p < .0001$) difference of the regression coefficient between P-QR under baseline and P-QR under zero flow in portal venous blood flow.

(Figure 2). During the generation of each P-Q relationship in the hepatic artery, Rha was calculated using the following equation:

$$Rha = (Pha - P_{Qha} = 0)/Qha. \quad (1)$$

Evaluation of HABR

The HABR was elicited by reducing Qpv from baseline to low flow produced by occlusion around the superior mesenteric artery. Systemic and regional hemodynamic parameters were obtained and hepatic arterial P-Q relationships were generated at baseline and at low flow in the portal vein. The magnitude of HABR was evaluated by comparing changes in hepatic arterial blood flow (ΔQha) with changes in portal venous blood flow (ΔQpv), using the index of change in blood flow (ΔQha/ΔQpv).

Experimental Protocol

Twenty-eight pigs were divided into three experimental groups: sevoflurane control group, SNP group, and NTG group. Twelve pigs were studied in SNP-administered condition, and nine pigs were studied in NTG-administered condition. Seven pigs were additionally studied in 4% sevoflurane anesthesia without administrating any exogenous NO donor in order to test the effect of mean arterial pressure on HABR. In all studies, 60 min was allowed for hemodynamic stabilization after surgical preparation. Anesthesia was then maintained with 2% sevoflurane plus 50% nitrous oxide and 50% oxygen (GOS). The hemodynamic

parameters and the baseline P-Q relationship were measured as the control period defined at baseline under GOS anesthesia after maintaining anesthesia for 30 min. In the SNP group ($n = 12$), SNP (3.0–5.0 $\mu g \cdot kg^{-1} \cdot min^{-1}$) was administered with reduction of systemic mean arterial pressure (mean $Psys_{art}$) (MAP, 60–80 mmHg). In the NTG group ($n = 9$), NTG (20–30 $\mu g \cdot kg^{-1} \cdot min^{-1}$) was administered with reduction of mean systemic arterial pressure (MAP, 60–80 mmHg). To test the effect of MAP itself, we used 4% sevoflurane plus 50% nitrous oxide anesthesia as a positive control. In the Sev4% group ($n = 7$), 4% sevoflurane plus 50% nitrous oxide and 50% oxygen was used for the maintenance of anesthesia to provide a consistent arterial pressure compared with SNP and NTG groups (MAP, 60–80 mmHg). Hemodynamic parameters and the P-Q relationship were determined after 30-min maintenance under reduced systemic mean arterial pressure conditions in both groups (Figure 2). After the experiment, the animals were deeply anesthetized with supplemental dose of i.v. injection of pentobarbital (20 mg kg^{-1}) under maintenance anesthesia (4% sevoflurane plus 50% nitrous oxide and 50% oxygen) and sacrificed by i.v. injection of KCL (40 meq/20 cc).

Statistical Analysis

A paired *t*-test was used to assess the effects of SNP and NTG on hemodynamic parameters, slopes of P-Q relationships, and hepatic arterial closing pressure ($P_{Qha=0}$) in the hepatic artery. The magnitude of HABR was statistically analyzed using the paired *t*-test. Values of $p < .05$ were considered statistically significant. Values are presented as mean ± standard deviation (SD).

RESULTS

Tables 1, 2, and 3 show systemic and regional hemodynamics of the hepatic artery and portal vein under baseline anesthesia and under administration of SNP, NTG, and 4% sevoflurane, respectively. With SNP and NTG, significant changes compared to the control condition were reflected in arterial hemodynamic changes, specifically with decreases in MAP, Rha, and $P_{Qha=0}$.

In brief, SNP reduced vascular tone in the systemic and hepatic arterial beds. MAP significantly ($p < .0001$) decreased from baseline (95.6 ± 3.8 mmHg) to SNP condition (68.3 ± 1.9 mmHg). The heart rate (HR) did not change from baseline (119.9 ± 6.6) compared to SNP condition (122.5 ± 3.8). Rha significantly decreased from baseline (11.7 ± 4.4 $mmHg \cdot ml^{-1} \cdot min \cdot kg^{-1}$) to SNP condition (9.1 ± 3.2 $mmHg \cdot ml^{-1} \cdot min \cdot kg^{-1}$).

Table 1. Systemic and regional hemodynamics in baseline and SNP conditions ($n = 12$)

	Baseline	SNP
$Psys_{art}$ (mean) (mmHg)	95.6 ± 3.8	68.3 ± 1.9*
HR (bpm)	119.9 ± 6.6	122.5 ± 3.8
CO ($ml \cdot min^{-1}$)	2670 ± 70	2290 ± 150*
Phv (mmHg)	4.5 ± 0.8	4.1 ± 0.9
Qpv ($ml \cdot min^{-1}$)	595.8 ± 65.8	489.6 ± 53.7
Ppv (mmHg)	9.3 ± 0.8	8.8 ± 0.8
Rpv ($mmHg \cdot ml^{-1} \cdot min \cdot kg^{-1}$)	0.12 ± 0.04	0.11 ± 0.08
Qha ($ml \cdot min^{-1}$)	192.0 ± 22.3	203.2 ± 29.5
Rha ($mmHg \cdot ml^{-1} \cdot min \cdot kg^{-1}$)	11.7 ± 4.4	9.1 ± 3.2*
$P_{Qha=0}$ (mmHg)	16.4 ± 1.3	13.1 ± 1.6*
Qpv + Qha ($ml \cdot min^{-1}$)	787.8 ± 75.9	692.5 ± 65.2
$P_{Qha=0}$ – Ppv (mmHg)	6.8 ± 1.2	4.3 ± 0.9*
Ppv – Phv (mmHg)	4.8 ± 0.6	4.7 ± 0.5

$Psys_{art}$ = mean systemic arterial pressure, HR = heart rate, CO = cardiac output, Qpv = portal venous blood flow, Ppv = portal venous pressure, Phv = hepatic venous pressure, Qha = hepatic arterial blood flow, Rha = hepatic arterial resistance, $P_{Qha=0}$ = hepatic arterial zero flow pressure; Qpv + Qha = total liver blood flow; $P_{Qha=0}$ – Ppv represents pressure gradient between $P_{Qha=0}$ and Ppv; Ppv – Phv represents pressure gradient between Ppv and Phv; *$p < .05$ vs. control value.

Table 2. Systemic and regional hemodynamics in baseline and NTG conditions ($n = 9$)

	Baseline	NTG
$Psys_{art}$ (mean) (mmHg)	92.7 ± 4.4	66.2 ± 1.7*
HR (bpm)	118.6 ± 3.9	119.7 ± 3.2
CO ($ml \cdot min^{-1}$)	2420 ± 60	2120 ± 40*
Phv (mmHg)	4.9 ± 0.5	4.3 ± 0.7
Qpv ($ml \cdot min^{-1}$)	521.1 ± 35.3	472.2 ± 45.0
Ppv (mmHg)	9.3 ± 0.6	8.6 ± 0.6
Rpv ($mmHg \cdot ml^{-1} \cdot min \cdot kg^{-1}$)	0.15 ± 0.09	0.17 ± 0.10
Qha ($ml \cdot min^{-1}$)	214.7 ± 45.0	372.6 ± 28.3
Rha ($mmHg \cdot ml^{-1} \cdot min \cdot kg^{-1}$)	10.7 ± 5.1	6.7 ± 2.8*
$P_{Qha=0}$ (mmHg)	17.2 ± 1.1	16.0 ± 1.2*
Qpv + Qha ($ml \cdot min^{-1}$)	733.8 ± 63.7	745.3 ± 55.4
$P_{Qha=0}$ – Ppv (mmHg)	7.9 ± 2.5	7.4 ± 1.4*
Ppv – Phv (mmHg)	4.7 ± 0.6	4.5 ± 0.5

$Psys_{art}$ = mean systemic arterial pressure, HR = heart rate, CO = cardiac output, Qpv = portal venous blood flow, Ppv = portal venous pressure, Phv = hepatic venous pressure, Qha = hepatic arterial blood flow, Rha = hepatic arterial resistance, $P_{Qha=0}$ = hepatic arterial zero flow pressure; Qpv + Qha = total liver blood flow; $P_{Qha=0}$ – Ppv represents pressure gradient between $P_{Qha=0}$ and Ppv; Ppv – Phv represents pressure gradient between Ppv and Phv; *$p < .05$ vs. control value.

Table 3. Systemic and regional hemodynamics in baseline and 4% sevoflurane conditions ($n = 7$)

	Baseline	4% Sevoflurane
$Psys_{art}$ (mean) (mmHg)	91.0 ± 2.8	71.9 ± 4.5*
HR (bpm)	102.0 ± 1.5	101.1 ± 0.8
CO (ml·min^{-1})	2150 ± 20	1810 ± 60*
Phv (mmHg)	4.3 ± 0.9	4.3 ± 0.7
Qpv (ml·min^{-1})	528.6 ± 20.6	486.0 ± 27.1
Ppv (mmHg)	8.3 ± 0.4	8.1 ± 0.5
Rpv (mmHg·ml^{-1}·min·kg^{-1})	0.18 ± 0.13	0.19 ± 0.18
Qha (ml·min^{-1})	194.3 ± 30.8	195.7 ± 32.9
Rha (mmHg·ml^{-1}·min·kg^{-1})	11.2 ± 4.7	8.8 ± 3.6*
$P_{Qha=0}$ (mmHg)	13.6 ± 1.6	14.6 ± 0.5*
Qpv + Qha (ml·min^{-1})	723.6 ± 20.7	681.7 ± 36.9
$P_{Qha=0}$ – Ppv (mmHg)	5.3 ± 1.8	6.5 ± 2.1*
Ppv – Phv (mmHg)	4.0 ± 1.1	3.6 ± 1.2

$Psys_{art}$ = mean systemic arterial pressure, HR = heart rate, CO = cardiac output, Qpv = portal venous blood flow, Ppv = portal venous pressure, Phv = hepatic venous pressure, Qha = hepatic arterial blood flow, Rha = hepatic arterial resistance, $P_{Qha=0}$ = hepatic arterial zero flow pressure; Qpv + Qha = total liver blood flow; $P_{Qha=0}$ – Ppv represents pressure gradient between $P_{Qha=0}$ and Ppv; Ppv – Phv represents pressure gradient between Ppv and Phv; *p <.05 vs. control value.

$P_{Qha=0}$ significantly decreased from baseline (16.4 ± 1.3 mmHg) to SNP condition (13.1 ± 1.6 mmHg). Pressure gradient across the liver ($P_{Qha=0}$ – Ppv) significantly decreased from baseline (6.8 ± 1.2 mmHg) to SNP condition (4.3 ± 0.9 mmHg).

In brief, NTG reduced vascular tone in the systemic and hepatic arterial beds. MAP significantly decreased from baseline (92.7 ± 4.4 mmHg) to NTG condition (66.2 ± 1.7 mmHg; $p < .0001$). The HR did not change from baseline (118.6 ± 3.9) compared to NTG condition (119.7 ± 3.2). Rha significantly decreased from baseline (10.7 ± 5.1 mmHg·ml^{-1}·min·kg^{-1}) to NTG condition (6.7 ± 2.8 mmHg·ml^{-1}·min·kg^{-1}). $P_{Qha=0}$ decreased significantly from baseline (17.2 ± 1.1 mmHg) to NTG condition (16.0 ± 1.2 mmHg). $P_{Qha=0}$ – Ppv significantly decreased from baseline (7.9 ± 2.5 mmHg) to NTG condition (7.4 ± 1.4 mmHg).

In brief, 4% sevoflurane reduced vascular tone in the systemic and hepatic arterial beds. MAP decreased significantly from baseline (91.0 ± 2.8 mmHg) to 4% sevoflurane condition (71.9 ± 14.5 mmHg; $p < .0001$). Rha decreased significantly from baseline (11.2 ± 4.7 mmHg·ml^{-1}·min·kg^{-1}) to 4% sevoflurane condition (8.8 ± 3.6 mmHg·ml^{-1}·min·kg^{-1}). $P_{Qha=0}$ increased from baseline (13.6 ± 1.6 mmHg) to 4 sevoflurane condition (14.6 ± 0.5 mmHg). $P_{Qha=0}$ – Ppv increased significantly from baseline (5.3 ± 1.8 mmHg) to 4% sevoflurane condition (6.5 ± 2.1 mmHg; $p < .05$).

Evaluation of the HABR is presented in Figure 3. Mean index of change in blood flow (ΔQha/ΔQpv) was also significantly increased from baseline (0.19 ± 0.12) to SNP condition (0.28 ± 0.17; $p = .009$) and from baseline (0.18 ± 0.17) to NTG (0.28 ± 0.20; $p < .05$). Mean index of change in blood flow (ΔQha/ΔQpv) decreased significantly from baseline (0.16 ± 0.12) to the 4% sevoflurane condition (0.09 ± 0.02; $p < .05$).

DISCUSSION

Mechanism of Potentiation by Exogenous NO Donors on HABR

Why exogenous NO donors SNP and NTG increased HABR gain compared to baseline remains unclear. Several possible mechanisms may explain this phenomenon.

The first mechanism may involve direct positive feedback of NO on adenosine release. Endogenous NO has been suggested to facilitate peripheral vascular adenosine-mediated dilation in the human forearm [13], while exogenous NO reportedly enhances adenosine release in the central nervous system [14–17]. Exogenous NO may thus enhance adenosine release in the space of Mall, augmenting HABR gain. Second, the interaction between NO and hydrogen sulfide (H_2S) should be noted. Other than adenosine, regulation of the HABR has been shown to further involve the gaseous inorganic compound H_2S [18]. Several studies support the existence of strong interactions between NO and H_2S to regulate vasorelaxation [19–21]. Third, changes in local regulation of mediators by changes in pressure gradient across the liver should be considered. Adenosine is thought to be constantly secreted into the fluid space of Mall, with the concentration of adenosine regulated by washout into the portal vein [22]. The pressure gradient across the liver circulation, i.e., hepatic artery, portal vein, and hepatic vein, may thus affect the efficiency of the "adenosine washout mechanism."

Clinical Implications

The use of exogenous NO donors may be of use in pathophysiological conditions such as endotoxemia and ischemia reperfusion injury. Sufficient levels of NO have been suggested to be important in preventing hepatic damage from endotoxemia [23]. Several studies have recently investigated the effects of systemic

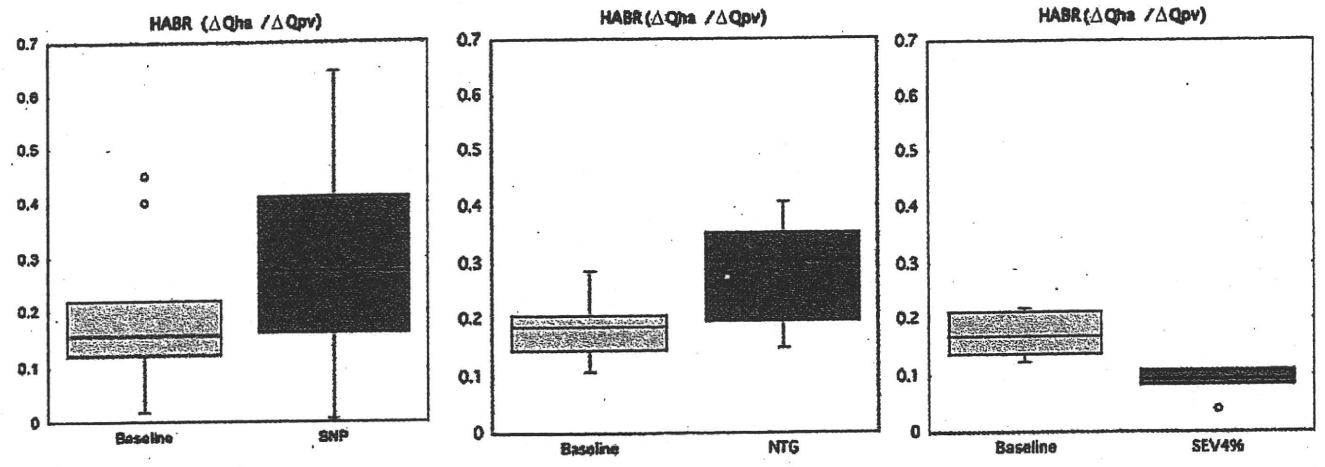

Figure 3. Effects of SNP, NTG, and 4% sevoflurane on magnitude of HABR. The HABR during baseline and with SNP, NTG, or 4% sevoflurane. The data was presented with mean ± SD.

application of NO donors in hepatic perfusion during early-stage endotoxemia [24–27]. Tamandl et al. [27] clearly suggested that the early administration of the NO donor SNP (3.0 $\mu g \cdot kg^{-1} \cdot min^{-1}$) into the portal vein during endotoxemia restores the HABR in a porcine model of endotoxemia. Furthermore, it has been reported by Chavez-Rivera et al. [28] that exogenous and endogenous NO, but not iNOS inhibition, improves the function and survival of ischemically injured livers. Most recently, Walsh et al. [29] and Phillips et al. [30] have suggested that NO may protect liver function against ischemia reperfusion injury. Our findings may provide additional information on the effect of systemic administration of SNP and NTG on HABR in a pathophysiological porcine model.

In conclusion, systemic administration of SNP or NTG in sevoflurane-anesthetized pigs increased the gain of the HABR (47–55%) in correlation with reduced vascular tone in the proximal hepatic arterial bed, probably via dilation of arterioles in the pre-sinusoidal compartment elicited by exogenous NO.

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DECLARATION OF INTEREST

The authors report no conflict of interest. The authors alone are responsible for the content and writing of this paper.

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