63 癌性貧血

cancer-related anemia

方　剤	構成生薬	条　文
人参養栄湯 (和剤局方)	地黄，当帰，白朮，茯苓，人参，桂皮，遠志，芍薬，陳皮，黄耆，甘草，五味子	脾肺俱ニ虚シ，発熱，悪寒，四肢倦怠，肌肉消痩，面黄，短気，食少ナク，濇を作シ，驚悸，自汗，若シクハ気血虚シテ諸症ヲ現ワスヲ治ス．
十全大補湯 (和剤局方)	黄耆，桂皮，地黄，芍薬，川芎，蒼朮，当帰，人参，茯苓，甘草	男子婦人，諸虚不足，五労七傷，飲食進マズ，久病虚損，時ニ潮熱ヲ発シ，気骨脊ヲ攻メ，拘急疼痛，夜夢遺精，面色癈黄，脚膝力無ク，一切病後，気旧ノ如カラズ，憂愁思傷，気血ヲ傷動シ，喘嗽中満，脾腎ノ気弱ク，五心煩熱スルヲ治ス．並ニ皆之ヲ治ス．此ノ薬性温ニシテ熱セズ．平補ニシテ効アリ．気ヲ養ヒ，神ヲ育シ，脾ヲ醒マシ，渇ヲ止メ，正ヲ順ラシ，邪ヲ避ク．脾胃ヲ温暖シテ其効具ニ述ブベカラズ．
加味帰脾湯	黄耆，柴胡，酸棗仁，蒼朮，人参，茯苓，竜眼肉，遠志，山梔子，大棗，当帰，甘草，生姜，木香	帰脾湯（済生方）：脾経ノ失血，少シ寝テ発熱盗汗シ，或ハ思慮シテ，脾ヲ破リ，血ヲ摂スルコト能ワズシテ以テ妄行ヲ致シ，或ハ健忘怔忡，驚悸シテ寝ネズ，或ハ心脾傷痛嚏臥少食，或ハ憂思シテ脾ヲ傷リ，血虚発熱シ，或ハ肢体痛ヲナシ，大便調ワズ，或ハ婦人経候不準，哺熱内熱，或ハ瘰癧流注シテ消散潰斂スルコト能ハザルヲ治ス．

● 疾患概念と背景

ここでいう**癌性貧血**とは，特に進行がん患者にみられる消耗性の貧血で，消化管出血や溶血など，明らかな原因が特定できない貧血をさす．このような病態にはインターロイキン-6(IL-6)などの炎症性サイトカインやヘプシジンが関与する．すなわち，がんも含めた慢性炎症状態ではIL-6によってヘプシジンの発現が亢進し，これが鉄のリサイクルを抑制して造血系への鉄の供給を減少させ，鉄欠乏性貧血に似た病態を惹

起する[1]．一方，進行・再発がんでは食欲低下による摂食不足から鉄欠乏性貧血がおこり，胃切除後には鉄およびビタミン B_{12} の吸収障害のため，前者では鉄欠乏性貧血，後者では巨赤芽球性貧血が発生する場合がある．

処方ガイド

癌性貧血には消耗性疾患から宿主を守る補剤（図 1）を中心に四物湯関連方剤が頻用される．四物湯に黄耆，桂皮を加えた十全大補湯・人参養栄湯が代表的である．十全大補湯は気虚と血虚の併存の場合に用いる．すなわち，易疲労感・動悸などの自覚症状，体重減少・皮膚乾燥などの他覚所見を使用目標にする．化学療法中にはこのような状態に陥る患者が多い．人参養栄湯も気虚と血虚が目標だが，不眠などの精神症状，息切れ・咳嗽・喀痰などの呼吸器症状，四肢の冷えなども重要な使用目標となる．加味帰脾湯は消化器機能改善による貧血の軽減をめざす方剤で，不安・緊張・焦燥感・不眠などの精神症状および微熱なども使用目標となる．なお，これらの漢方薬服用後に悪心・下痢がみられた場合は副作用として対応するべきである．

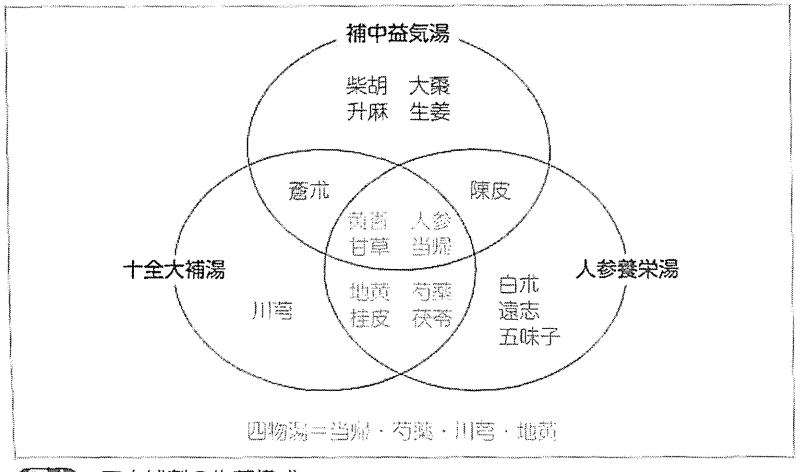

図 1　三大補剤の生薬構成

漢方薬の作用機序

十全大補湯は実験的に造血幹細胞を増加させ，脾臓内でのコロニーの数と大きさを増やす作用が証明されている[2]．人参養栄湯にはリバビリンによる溶血性貧血の軽減作用がある[3]．十全大補湯では，補中益気湯と共通の黄耆，蒼朮，当帰，人参，甘草によって消化器機能改善による補気作用を基盤に，地黄，芍薬，川芎，茯苓による造血能亢進作用と桂皮による血行動態の改善作用により，気血双補効果が達成される．放射線照射マウスの骨髄回復機能をみた実験的研究[4]で，人参養栄湯は赤血球・白血球・血小板の 3 系統すべての回復作用を示し，骨髄における前駆細胞の増殖・分化を促進する作用がある．この他には鉄欠乏性貧血における鉄の吸収促進作用がある．

ピットフォール

漢方のみで癌性貧血に対応できない．ヘモグロビン濃度が 7.0 g/dL 以下になったら，漢方治療にこだわることなく，輸血をためらうべきではない．

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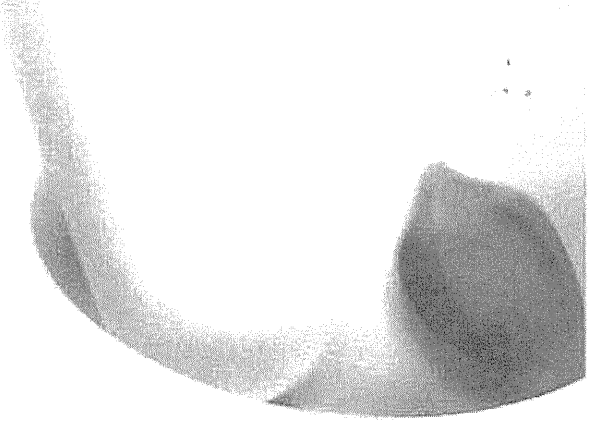
（元雄良治）

“治せる”医師をめざす

方剤別 はじめての 漢方100

―個別医療を実現するためのさじ加減の極意―

後山 尚久
大阪医科大学健康科学クリニック



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目次

11 小柴胡湯（しょうさいことう）

四逆散類　四君子湯類　陽証　虚実中間証　和解剤

生　薬		含有量	作　用
柴胡	㊐寒	5.0-8.0	解熱・消炎
黄芩	㊐寒	2.5-3.0	解熱・消炎・止血
半夏	㊙温	3.5-8.0	鎮吐・去痰・平喘
甘草	㊓平	1.0-3.0	緩和・止渇
人参	㊙温	2.5-3.0	興奮・強壮・強精
生姜	㊙温	1.0-2.0	発散・健胃・鎮吐
大棗	㊙温	2.5-3.0	強壮・緩和・鎮静

適　用

疾患・症状　諸種の急性熱性疾患（肺炎，気管支炎，感冒[1]など）／肺結核や結核性胸膜炎などの結核性諸疾患の補助療法／リンパ節炎／慢性胃腸障害／産後回復不全／慢性肝炎／めまい[45]／口苦／頸項部の強ばり／咽頭の乾燥感[47]／食欲不振／悪心／往来寒熱

適応症としては，呼吸器疾患・消化器疾患を中心にかなりいろいろな疾患が含まれるが，小柴胡湯は慢性肝炎患者に多く使われた時期があり，1990年代に間質性肺炎による死亡例が出てから，慢性肝炎に使用されることが激減した[1]．特にインターフェロンとの併用や慢性肝炎で血小板数が10万/mm^3以下の例・肝硬変・肝細胞がんの患者への投与は禁忌となっている．C型慢性肝炎の治療では抗ウイルス療法の進歩があり，小柴胡湯を積極的に使用することは少なくなったが，抗ウイルス療法無効例あるいはアレルギーや副作用のために治療が困難例には，証を吟味したうえで，小柴胡湯を投与できる例は存在するであろう．

漢方症候　舌候：紅味あり・湿潤・薄い白苔，脈候：弦，腹候：胸脇苦満（現代では右胸脇苦満が強いとされるが，古典ではむしろ左が多いと記載[2]），心下痞鞕（しんかひこう），中等度の腹直筋緊張．

漢方医学的には少陽病期の代表的方剤である．前述の疾患・症状から，亜急性および慢性の各種炎症性疾患に応用可能である．

類似方剤の使いわけ

少陽病期の虚実中間証では，次のような方剤がある（カッコ内はその証の特徴）

- **四逆散**（精神不安・物事へのこだわり・四肢の冷え・両側腹直筋肉の緊張）
- **柴胡疎肝湯**（腹腔内ガスによる諸症状・抑うつ傾向）
  また下記の方剤は虚実は異なるが，重要な類似方剤である．
- **大柴胡湯**：より実証で，便秘を伴い，胸脇苦満と心下痞鞕の程度が強い点が使用目標となる．六病位では少陽病期から陽明病期に移行しつつあるような病態である（裏熱実証）．小柴胡湯が和解剤であるのに対して，大柴胡湯は表裏双解剤（表裏）．
- **柴胡加竜骨牡蠣湯**：より実証で，自覚症状としては，不眠・イライラ感・不安などの精神神経症状（煩驚）を伴い，他覚所見としては胸脇苦満と心下悸を使用目標にする．高ストレス下の交感神経緊張による高血圧患者には適している．
- **柴胡桂枝湯**：より虚証で，六病位では太陽病期から少陽病期への移行期で，自覚的には肩こり・首から上の発汗，他覚的には胸脇苦満に加えて両側腹直筋緊張（腹皮拘急）が特徴的である．気逆を伴う病態と考えられる．

構成生薬からみた方剤の特徴

君臣佐使は成無己「傷寒明理薬方論」に拠った．君薬の柴胡はトリテルペン系サポニンであるサイコサポニンa～fなどを含み，抗炎症作用を持つ．漢方医学的には解表（げひょう）剤で発汗・発散を促す，辛涼解表（しんりょうげひょう）薬である（冷やしながら解表する）．少陽病期の主薬であり，胸脇の気滞を散じる．

臣薬の黄芩は清熱燥湿（せいねつそうしつ）薬であり（乾燥しながら熱を除去する），解熱・消炎・止血作用を有する．特にこれら柴胡と黄芩は少陽病期の半表半裏

の熱を散ずるとされる．柴胡の成分であるサイコサポニンや黄芩の成分であるバイカリン・バイカレインには肝がん細胞の増殖抑制作用のあることについて筆者ら[3]およびその他の報告がある．臨床的にも小柴胡湯の肝がん発生抑制効果が報告されているが，肝硬変患者には小柴胡湯が使えない．しかし，これまでの基礎的・臨床的研究は決して無駄ではなく，小柴胡湯の合方や関連方剤の肝がん発生抑制効果を念頭に診療に応用できるであろう．

佐薬のうち半夏は，化痰止咳平喘薬に分類され，咳・痰・喘息に用いられる温化寒痰薬である（寒性の痰を除く），健脾和胃・鎮吐・去痰・平喘作用を有する．人参は，「補薬の王」ともよばれ，興奮・強壮・強精・大補元気・安神益智・建脾益気・生津作用を有する．甘草は緩和・止渇・止痛作用を有する．人参・甘草はともに正気を補い，中を和する．

使薬のうち生姜は解表剤（発汗・発散を促す），辛温解表薬であり（温めながら解表する），発散・健胃・鎮吐・鎮嘔・食欲増進・発汗解表・鎮咳作用がある．大棗は補脾胃・強壮・養血・安神・緩和・鎮静作用がある．生姜・大棗で脾胃を補う．

小柴胡湯全体の生薬構成を俯瞰すると，柴胡・黄芩・半夏は攻撃，人参・甘草・大棗・生姜は防御，と攻守のバランスが取れており，和解の主方とされている．

さじ加減　（🔄：入れ替え，⬇：減量，⬆：増量，➕：合方（加方），➖：減方）

臨床的には，小柴胡湯合桂枝湯である柴胡桂枝湯が，急性炎症からやや時間が経過した段階（六病位のうち太陽病から少陽病への移行期）に用いると奏効する．柴胡桂枝湯は慢性膵炎[4]，慢性肝炎，慢性胃炎などの経過観察に用いることが多く，特にアルコール性肝障害患者には，これ1剤で胃・肝臓・膵臓を保護する意味で対応できる．柴胡桂枝湯の慢性膵炎治療効果の機序には抗炎症・抗アポトーシス・抗線維化・抗酸化の四つの作用があることを筆者らが報告している[4]．

小柴胡湯合半夏厚朴湯である柴朴湯は咽喉頭異常感症の治療薬として有名であり，耳鼻咽喉科や消化器科の医師も処方する．また本来の呼吸器疾患，特に気管支喘息の治療薬あるいは補助薬として呼吸器領域で用いられる．

小柴胡湯合五苓散である柴苓湯は，漢方のステロイドとも称され，自己免疫性疾患，および免疫が関与する諸疾患において，疾患自体への治療効果およびステロイドの減量に寄与している．ここで重要な点は，ステロイドの適応である状況では適切にステロイドを使用することである．そしてステロイドが奏効した際には，ステロイドの漸減過程において柴苓湯を併用しながら，上手にステロイド減量を図ることができる．人工股関節全置換術後の下腿浮腫と炎症に対する柴苓湯の有効性をランダム化比較試験（RCT）で検証した報告がある[5]．ネフローゼ症候群，特に小児期の IgA 腎症への有効性も明らかにされている．

小柴胡湯加桔梗石膏は，文字通り，桔梗の扁桃腺への作用と，強い抗炎症作用を有する石膏を加味した小柴胡湯加味方であり，扁桃炎，扁桃周囲炎に用いられる．

また，黄疸が遷延するような肝機能障害患者に小柴胡湯と茵蔯五苓散の併用がなされる．

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（元雄良治）

38 大柴胡湯（だいさいことう）

四逆散類　陽実証　和解剤

生薬		含有量	作用
柴胡	君寒	6.0-8.0	解熱・消炎
黄芩	臣寒	3.0	解熱・消炎・止血
芍薬	佐涼	3.0	鎮痛・鎮痙
枳実	佐寒	2.0-3.0	瀉下・健胃
大棗	使温	3.0-4.0	強壮・緩和・鎮静
半夏	使温	2.5-8.0	鎮吐・去痰・平喘
生姜	使温	1.0-2.0	発散・健胃・鎮吐
大黄	使寒	1.0-2.0	瀉下・利胆・消炎・健胃

適　用

疾患・症状　胃炎[11]／脂肪肝／胆石症／高血圧／肥満症[18]／糖尿病／便秘症／神経症／不眠症／うつ状態／蕁麻疹／肩こり[49]／頭痛／耳鳴／のぼせ傾向／上腹部が張って苦しい／不眠・イライラ感などの精神症状／悪心・嘔吐／めまい

消化器を中心に，メタボリックシンドロームの基準を満たすような疾患に用いられ，精神神経疾患に応用できる点が特徴的である．脂肪肝には近年増加傾向の非アルコール性脂肪肝炎(NASH)／非アルコール性脂肪肝疾患(NAFLD)なども含まれ，よく問診すると不眠やイライラ感などの精神神経症状が明らかになることが多い．胆石，特に非石灰化結石には，ウルソデオキシコール酸(UDCA)600 mg/日に大柴胡湯を併用してもよい．大柴胡湯のみで胆石が消失した例もあるので，UDCAのみでは効果不十分と考えられた場合や，胆石・胆嚢炎に伴う諸症状・精神神経症状に対処したい場合に大柴胡湯の適応となる[1]．上述のように，精神神経症状・耳鼻科的症状・消化器症状が中心となる．

漢方証候　舌候：白色～黄色の厚い苔があることが多い，脈候：弦・数で力がある，腹候：両側の広範囲な胸脇苦満・心下急(みぞおちが張る)．

類似方剤の使いわけ

大柴胡湯は少陽～陽明病期の実証の方剤であり(裏熱実証)，類似の方剤としては，次のような方剤がある．

- **小柴胡湯**：やや虚証，便秘なし
- **柴胡加竜骨牡蠣湯**：抑うつ・不安・易怒性などの精神神経症状が強く，臍上悸著明
- **四逆散**：精神不安・物事へのこだわり・四肢の冷え・腹皮拘急著明
- **茵蔯蒿湯**：心下痞が著明，黄疸，腹部膨満
- **木防己湯**：心下痞堅，顔色不良，浮腫傾向
- **防風通聖散**：体力充実・肥満・高血圧などは共通するが，胸脇苦満は伴わない．
- **柴胡桂枝湯**：易怒性は共通するが，やや虚証で，胸脇苦満はより軽度で，口苦・発汗傾向を伴う．

構成生薬からみた方剤の特徴

君臣佐使は成無己「傷寒明理薬方論」に拠った．大柴胡湯は小柴胡湯から人参・甘草を去り，大黄・枳実・芍薬を加えたもので，臓腑の実を去る作用を有する．

君薬の柴胡および臣薬の黄芩については小柴胡湯の項(p.42)を参照されたい．これらの2生薬は清熱・疎肝作用により，胸脇苦満を去る．なお大黄を含まない大柴胡湯エキス製剤もある．

佐薬のうち，枳実は破気消積，化痰除痞の作用，すなわち理気作用が強く，破気(気鬱散開)の効能がある．食積停滞による腹痛・便通異常の証候，あるいは痰濁が気機を阻むことによる胸・心下の痞えに用いる．生薬成分としては，ヘスペリジン，ナリンギン，シネフリンなどを含み，芳香性健胃作用・抗アレルギー作用を有する．動物実験では，消化管蠕動運動の促進・蠕動運動のリズム調節などが報告されている．枳実は子

宮収縮力を増強し，緊張度を高めることから，子宮脱に枳実を使用する科学的根拠となっている．そのほかには，血圧上昇・心筋収縮力調整(低濃度で収縮を増強し，高濃度で収縮を弱める)．芍薬は肝火を瀉し，陰気を収斂する．生薬成分としてはモノテルペン配糖体であるペオニフロリンなどがあり，薬理作用としては鎮痛作用・抗炎症作用・平滑筋弛緩作用があげられる．これらの２生薬は堅を除き，積を破るとされ，大黄とともに内熱を下し，心下急を去る．

使薬のうち，半夏・生姜は堅を散じて，胃を和し，嘔気を止める．大棗は営衛を調え，胃を緩くし，脾を益する．大黄は瀉下・通便作用により，実熱を瀉し，積滞を下す．

なお，大柴胡湯の胆石溶解作用の機序としては，腸管でのコレステロール吸収抑制・肝臓でのコレステロール合成抑制・胆汁酸への異化亢進により，胆汁中コレステロール飽和度を低下させ，胆石形成を抑制すると考えられている[2]．

また，高脂肪食マウスにおける高脂血症・脂肪肝に対する大柴胡湯の効果についての実験的な研究も報告されており[3]，まさに現代人の生活習慣によって増加傾向にあるこれらの疾患において，大柴胡湯の果たす役割は大きい．

さじ加減　(🔄：入れ替え，➖：減量，➕：増量，➕：合方(加方)，➖：減方)

大柴胡湯はおもに高脂血症，脂肪肝を伴う肥満症に使うことが多い．さらには胆石症にも用いられる．小柴胡湯との鑑別は，明らかに実証であれば大柴胡湯を用い，同じ柴胡剤であれば四逆散よりはさらに胸脇苦満が強い例に用いる．実際の診療現場では，不眠・便秘傾向の合併を使用目標にしている．

アルコール性肝障害あるいは胆石症などでは，慢性膵炎あるいは胃腸症状を訴える例がある．このような例には柴胡桂枝湯が用いられることが多いが，明らかな脂肪肝がおもな病態であれば大柴胡湯が用いられる．

大柴胡湯去大黄は，大柴胡湯の証にほぼ合致するが，軟便でやや虚証の例に用いる．

清熱瀉火の黄連解毒湯と補血活血の四物湯の合方が温清飲で，さらに柴胡・薄荷・桔梗・牛蒡子・栝楼根を加えたものが柴胡清肝湯である．少陽病期で裏熱だが，虚証の小児の神経症・慢性扁桃腺炎・湿疹に用いる．

「類似方剤の使いわけ」で述べた柴胡加竜骨牡蠣湯は，実証で，精神不安やイライラ感などの精神神経症状を呈し，胸脇苦満を伴うが，生薬構成としては，柴胡・黄芩・半夏・大棗・生姜が大柴胡湯と共通し，柴胡加竜骨牡蠣湯にのみ含まれる生薬は桂皮・牡蠣・茯苓・人参・竜骨である．竜骨・牡蠣は鎮静効果が強く，精神安定作用があり，ほかも鎮静効果を有する生薬が協働している．また人参・大棗のような補脾作用を持つ生薬も配して，全体として脾気虚に心肝火旺が加わった病態に対応する方剤である．

大柴胡湯合桃核承気湯・大柴胡湯合桂枝茯苓丸は，漢方医学的には大柴胡湯の証に瘀血の病態が明瞭に出ている場合に用いる．実際の診療場面では，過食傾向のある肥満症で，高尿酸血症・痛風などを合併している例に用いることが多い．

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Research Article

Study of Factors Involved in Tongue Color Diagnosis by Kampo Medical Practitioners Using the Farnsworth-Munsell 100 Hue Test and Tongue Color Images

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In traditional Japanese medicine (Kampo medicine), tongue color is important in discerning a patient's constitution and medical conditions. However, tongue color diagnosis is susceptible to the subjective factors of the observer. To investigate factors involved in tongue color diagnosis, both color discrimination and tongue color diagnosis were researched in 68 Kampo medical practitioners. Color discrimination was studied by the Farnsworth-Munsell 100 Hue test, and tongue color diagnosis was studied by 84 tongue images. We found that overall color discrimination worsened with aging. However, the color discrimination related to tongue color regions was maintained in subjects with 10 or more years of Kampo experience. On the other hand, tongue color diagnosis significantly differed between subjects with <10 years of experience and ≥10 years of experience. Practitioners with ≥10 years of experience could maintain a consistent diagnosis of tongue color regardless of their age.

1. Introduction

In traditional Japanese medicine (Kampo medicine), observing the tongue shapes and colors is a method for diagnosing the patient's constitution and medical conditions. In addition to the information that the tongue reveals, Kampo evaluations are supplemented with data from questionnaires, pulse, and abdominal diagnosis. Tongue diagnosis is particularly useful for detecting *Mibyou*, the "disease-oriented" healthy stage in Kampo medicine. Kampo tongue information, such as tongue pain in the dental oral area, can be used to prevent potentially refractory diseases [1, 2]. Generally, tongue diagnosis focuses on tongue texture and tongue coating. The colors and shapes of each part can be investigated to diagnose medical conditions.

Mainly, tongue color is the result of light reflection and light absorption. The color of the tongue (tongue color) is especially dependent on internally diffused light. Tongue color diagnosis (TCD) can provide very useful information for medical conditions. By TCD, we can get useful information about the patient's reservoirs of heat and cold, exhaustion level, mental state, digestive system function, blood circulation dynamics, and water metabolic state. However, tongue color diagnosis is affected by two types of factors. One is environmental factors, such as light sources or room temperature, which influence impact diagnosis. The other type includes the subjective factors of the observers, especially their knowledge of Kampo and experience using it.

In recent years, to solve the problem of environmental factors (EF), many researchers have developed a tongue imaging system that operates at constant conditions [3–6]. Chiu devised the hardware and software for tongue imaging and examined the tongue surface and tongue coating, divided into areas related to concepts of traditional medicine [3]. Wang et al. introduced a method of evaluating the color of

the tongue surface, dividing the tongue into different regions and excluding the tongue coating [4, 5]. Zhang et al. devised a system for tongue imaging and quantifying the tongue image information, considering both measurement values and the patient's past medical history [6]. Kanawong et al. compared the color value of tongue images with the patient's hot or cold condition [7]. In addition, they measured the RBG value of tongue images obtained in the same imaging environment and evaluated the tongue color quantitatively then used those data for early detection of diseases such as appendicitis and liver cancer [8, 9]. We first undertook research to standardize tongue diagnosis in 2008. As one of our research outcomes, we have been developing a new tongue imaging method and diagnostic support system (Tongue Image Analyzing System (TIAS)) for performing tongue diagnosis. The key characteristic of the tongue imaging method in TIAS is the exclusion of the influence of external light using an integrating sphere to achieve an evenly distributed light intensity with a halogen light source (Moritex Inc., MHAB-150W, color temperature 3200 K). Further, TIAS can remove the gloss of the tongue surface from its images. Our prior study investigated the use of spectral camera imaging [10]. We confirmed the relationships between the Kampo concept of *Oketsu* and both liver function and thyroid function in blood samples as measured by wavelength values [11–13]. Subsequently, in aiming to further promote TIAS, we changed from a spectral camera to a digital camera (Lumenera Inc., Lw115C, 1280 × 1024 pixels, Color CMOS sensor), although we are still using the basic data from the spectral camera. We changed because digital cameras are cheap and the color is superior for viewing purposes. For the quantitative measurement methods in TIAS, RGB values of digital camera images were converted into CIE1976 $L*a*b*$ color space values. Imaging by TIAS was confirmed to be stable for 3 weeks [14]. As mentioned above, our method has made it possible to perform stable quantitative measurement of tongue images by TIAS, and we have almost solved the problem of EF.

As far as we know, there are no other reports about subjective factors (SF) in TCD; the problem of SF has remained unclear. In tongue color diagnosis, age, gender, difference in color discrimination, and experience and knowledge in Kampo medicine are thought to be important influences. Thus, we set out to examine the influence of these factors. We studied the relation of age, gender, color discrimination, and duration of Kampo experience on TCD. One method to evaluate color discrimination is the Farnsworth-Munsell 100 Hue test (Hue test). The Hue test has been used for many years in industrial fields to check color discrimination. In various other fields, many studies on color discrimination have been reported using the Hue test. [15, 16]. The Hue test was evaluated for color discrimination of patients with optic neuritis in ophthalmology [17, 18]. And, the Hue test has been used by neuroscientists to study color discrimination and occipital lobe function in patients with Parkinson's disease and pituitary adenoma [19–21]. The Hue test was first devised by Farnsworth in 1943, and the present 85 colored-caps version was improved in 1957 [22]. The color caps are divided into four hues, and the 85 caps are arranged into four boxes, each containing a fixed anchor cap at both ends of each box. One box consists of 22 caps, and the other three boxes consist of 21 caps each. Color discrimination is evaluated when the subject attempts to arrange the caps into the correct hue order. The total Hue score is calculated by the number of misplacements. Thus, a lower Hue score indicates better color discrimination.

The purpose of this study was to reveal the SF involved in Kampo tongue diagnosis. We recorded data about age, gender, duration of Kampo experience, and primary occupations in Kampo medical practitioners. We evaluated color discrimination by the Hue test. Simultaneously, we examined the individual discrepancies in TCD using tongue images in which the color was adjusted by computer processing, and we studied the relationships of age, gender, color discrimination, and duration of Kampo experience with these results.

2. Subjects and Methods

2.1. Subjects. The subjects were 68 Kampo medical practitioners (48 males, 20 females). First, we questioned the subjects about their age, gender, duration of Kampo experience, and primary occupation. In order to maintain advanced color reproducibility, we had to exclude the influence of external light in the experimental environment. Thus, the experiments were conducted in a dark room (Figure 1). All subjects continuously performed the Hue test and TCD using tongue images.

2.2. Hue Test. We used artificial solar illumination (SERIC Inc., XC-19, 5500K) for the Farnsworth-Munsell 100 Hue test (SAKATA Inc., Farnsworth-Munsell 100 Hue test Munsell color) (Figure 2). The illumination was set on the ceiling of the darkroom, so that the angle of illumination could be about 90° and the angle of viewing could be about 60°. The subjects were ordered to rearrange the color caps of one color phase placed randomly in one slim-line box in correct order in two minutes. They performed this task on all four color phases; that is, they completed the Hue test. We calculated the Hue score according to the number of caps rearranged incorrectly compared with the correct orders of color phases. There were three levels of color discrimination ability: the superior-ability group (Hue score 0–16), normal-ability group (Hue score 20–100), and low-ability group (Hue score more than 100) [22]. In addition, we measured actual values of all the color caps in CIE 1976 $L*a*b*$ color space using the spectroradiometer (KONICA MINOLTA Inc., CS-1000A) in the experimental environment. The result shows that the tongue colors used in this experiment corresponded to those of color caps number 64–78 in CIE 1976 $L*a*b*$ color space (Figure 2). Therefore, we established a tongue color region (TCR) as the number 64–78 color caps region, and we also examined the relation between each influence factor and TCR.

2.3. Tongue Color Diagnosis (TCD) of Tongue Images. In creating the tongue color images, we used 1551 tongue images taken by TIAS. In order to determine the distribution of

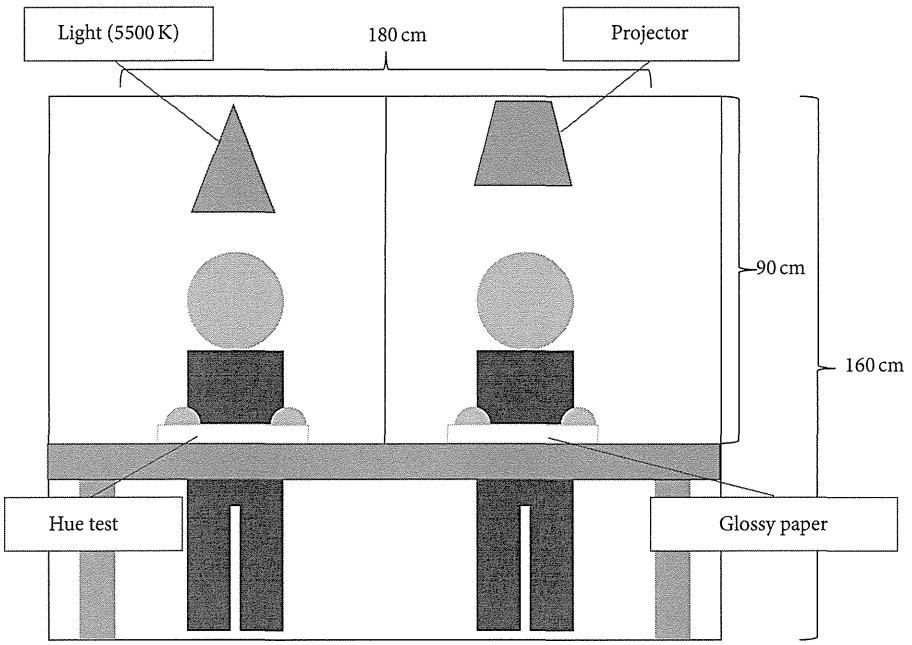

FIGURE 1: The experimental environment in this study. The experiments were conducted in a dark room with a single light source. For the Hue test, the light was positioned above so that the angle of illumination would be 90° and the angle of Hue test viewing would be approximately 60°. For the tongue color diagnosis, full-color tongue images were projected onto glossy paper by a projector.

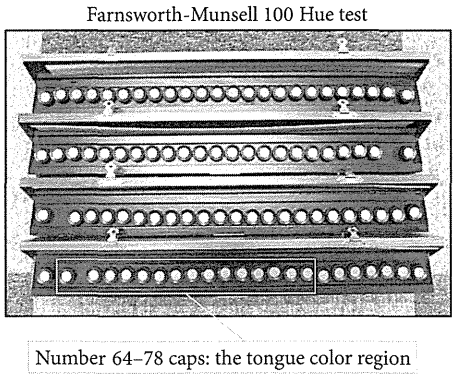

FIGURE 2: Color discrimination was evaluated by the Farnsworth-Munsell 100 Hue Test. The color discrimination is evaluated based on the subject's attempt to rearrange the caps into the correct hue order. Total Hue scores are calculated as the number of misplacements, and a lower score therefore indicates better color discrimination. The tongue color regions (TCRs) correspond to caps number 64–78.

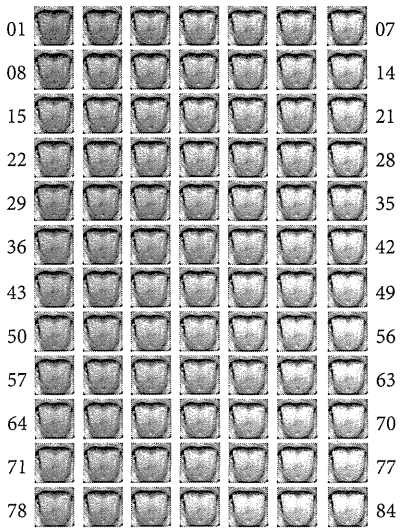

FIGURE 3: Tongue images 01–84.

the colors of the 1551 tongue images, we performed principal component analysis. By determining the color using principal component axes, it was possible to set the color gamut of the tongue without deviating far from the tongue color. The distance of the color becomes a constant interval by dividing the tongue color gamut into a 7 : 4 : 3 ratios and the 84 (7 × 4 × 3) tongue images were obtained from it (images 01–84: Figure 3). Furthermore, we measured actual values of the tongue colors on the tongue image color chart in CIE 1976 $L*a*b*$ color space in an experimental environment. The tongue color images were projected onto glossy paper by a projector (EPSON Inc., EB-1761W), and subjects were asked to diagnose the tongue color in each of the 84 tongue images. The color of the TCD was selected from among five designations: pale, pale red, red, crimson, and purple (Figure 4) [23].

2.4. The Ethics and Statistical Analysis. We obtained informed consent for this experiment from all subjects using descriptive text.

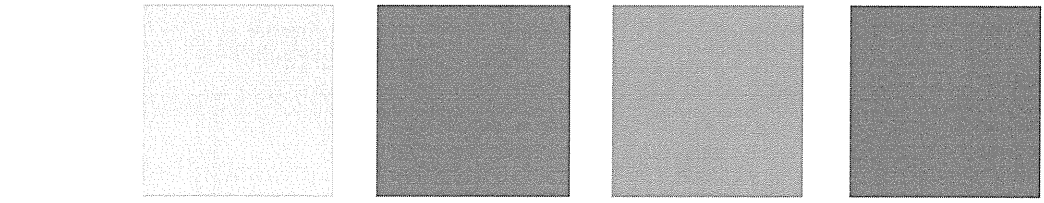

FIGURE 4: Tongue color diagnosis included five colors: pale, pale red, red, crimson, and purple.

TABLE 1: Comparison of duration of Kampo experience with subjects' age, gender, and occupation.

	Duration of Kampo experience		P value
	<10 years	≧10 years	
Age			
<43 years	26	5	0.000**
≥43 years	9	28	0.001**
Gender			
Male	19	29	0.099
Female	16	4	0.011*
Occupation			
M.D.	22	30	0.186
Not M.D.	13	3	0.017*

M.D.: medical doctor.
All P values were obtained by χ^2-test. $^*P < 0.05$, $^{**}P < 0.01$.

The data were analyzed by Student's t-test when they were assumed to be homoscedastic by the F-test. If the data could not be assumed to be homoscedastic by the F-test, they were analyzed by Welch's test. When the data were not consecutive variables, they were analyzed by the χ^2-test. In each analysis, the significance level was set at less than 5%. We used the Pearson product-moment correlation coefficient.

3. Results

3.1. Subjects. In this study, we obtained data from 68 Kampo medical practitioners. Their ages ranged from 27 to 69. The average age was 44.3 ± 9.1 among all subjects, 45.9 ± 8.9 among males and 40.5 ± 8.4 among females; the median age was 43. The subjects' duration of Kampo medical experience averaged 12.1 ± 9.5 years, ranged from 1 to 40, and had a median value of 10. The subjects consisted of 52 medical doctors, 6 acupuncturists, and 10 pharmacists who made tongue diagnosis in daily operations (Table 1). There was a positive correlation between the ages and the duration of Kampo medical experience ($r = 0.753$). There were fewer females than males in the age group ≥43 years and in the group with ≥10 years of Kampo medical experience.

3.2. Hue Test Color Discrimination in the Entire Region and the Number 64–78 Region. The entire region of Hue scores (EHS) ranged from 4 to 138, with an average of 39.2 ± 25.4 and median value of 30. There were 12 subjects with superior ability, 54 subjects with normal ability, and 2 subjects with low ability of color discrimination according to the Hue score. The Hue scores for the number 64–78 caps ranged from 0 to 36, with an average of 4.4 ± 6.6, and a median value of 2.

EHSs were analyzed in terms of age, gender, and duration of Kampo medical experience. The group of <43 years old ($n = 31$) had a significantly lower EHS average (better color discrimination) than those ≥43 years old ($n = 37$) (t-test, $P = 0.012$) (Figure 5(a)). With regard to gender, there was no significant difference between the number of men and women in the groups with scores <30 and ≥30, stratified by age (Figure 5(b)). There was no significant difference between the rate of inexperienced (<10 years) and experienced (≥10 years) Kampo practitioners in the groups with scores of <30 ($n = 30$) and ≥30 ($n = 38$) stratified by age (Figure 6(a)).

The number 64–78 region of Hue scores (64–78 HS) was considered to correspond to the TCR. In the same way as described for EHSs above, 64–78 HS were analyzed with regard to age, gender, and duration of Kampo experience. No significant difference in the 64–78 HS between the age groups <43 years ($n = 31$) and ≥43 years ($n = 37$) was found (t-test, $P = 0.257$). Analyzing the mean 64–78 HS for each gender in each age group, no significant difference was found between males and females. In terms of Kampo experience, we compared the ratios of experienced (≥10 years) and inexperienced (<10 years) Kampo practitioners in the group with 64–78 HS < 2 ($n = 33$) and that with 64–78 HS ≥ 2 ($n = 35$) (Figure 6(b)). A significant difference was found in the ratios in each score category between the two groups (χ^2-test, $P < 0.01$). In workers with <10 years of Kampo experience, age had a deleterious effect on color discrimination, with those >30 years old having a smaller ratio of good 64–78 HS scores (64–78 HS < 2). However, in the group with ≥10 years of Kampo experience, the ratio of 64–78 HS < 2 did not decrease. This tongue-color-specific region was the only one for which significant differences in color discrimination were found between workers with Kampo experience for <10 years and those with Kampo experience for ≥10 years; furthermore, in other color regions, Hue scores uniformly increased with aging.

3.3. Tongue Color Diagnosis of Tongue Images. We examined the total number of answers of each tongue color for TCD of the tongue images (images 1–84) projected onto glossy paper. The total number of answers was 5712 (84 images × 68 subjects). The cumulative numbers of answers of each tongue color were as follows: pale 1265, pale red 1536, red

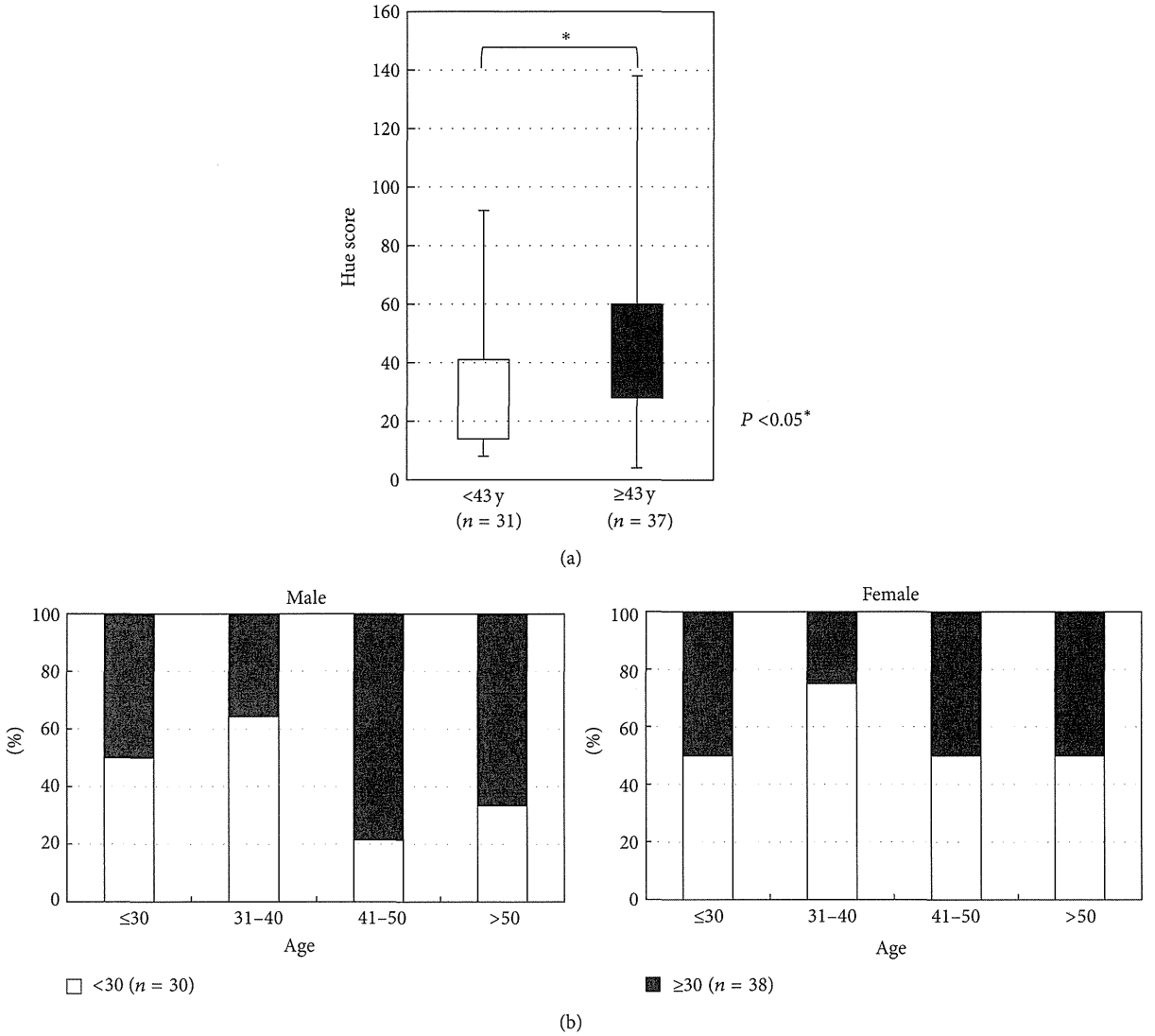

FIGURE 5: (a) The <43 years group had significantly lower average Hue scores than the ≥43 years age group (t-test, $P = 0.012$). (b) The rate of subjects with Hue scores of <30 and ≥30 was compared between genders and separated by age. There were no significant differences between males and females.

1482, crimson 1142, and purple 287. For each tongue color we compared the answer distributions with regard to age, gender, color discrimination (EHS and 64–78 HS scores), and duration of Kampo experience. There were no significant differences between age, gender, and color discrimination abilities (EHS and 64–78 HS scores) for TCD of the tongue images. However, the distribution of TCD was significantly different between workers with <10 years of Kampo experience ($n = 35$) and those with ≥10 years of experience ($n = 33$) (χ^2-test, $P < 0.01$) (Figure 7). Incidentally, there was no significant difference between other durations of Kampo experience. Further, we examined the relationship with TCD of the 64–78 HS groups and the duration of Kampo experience. TCDs were compared for the groups with 64–78 HS < 2 ($n = 18$) and 64–78 HS ≥ 2 ($n = 17$), first in the group with <10 years of Kampo experience, and then in the group with ≥10 years of Kampo experience (Figure 8). As a result, the distribution of TCD was significantly different between 64–78 HS < 2 and ≥2 in workers with <10 years of Kampo experience (χ^2-test, $P < 0.01$), but not for with ≥ 10 years of Kampo experience.

4. Discussion

We studied the relationships between color discrimination on the one hand and age, gender, and duration of Kampo experience on the other. We found that overall color discrimination was associated with age but that the color discrimination of the tongue color region (TCR) was associated with duration of Kampo experience. Further, we found that duration of Kampo experience influenced TCD.

TCD and color discrimination measurement require high color reproducibility. The reason is that color is determined

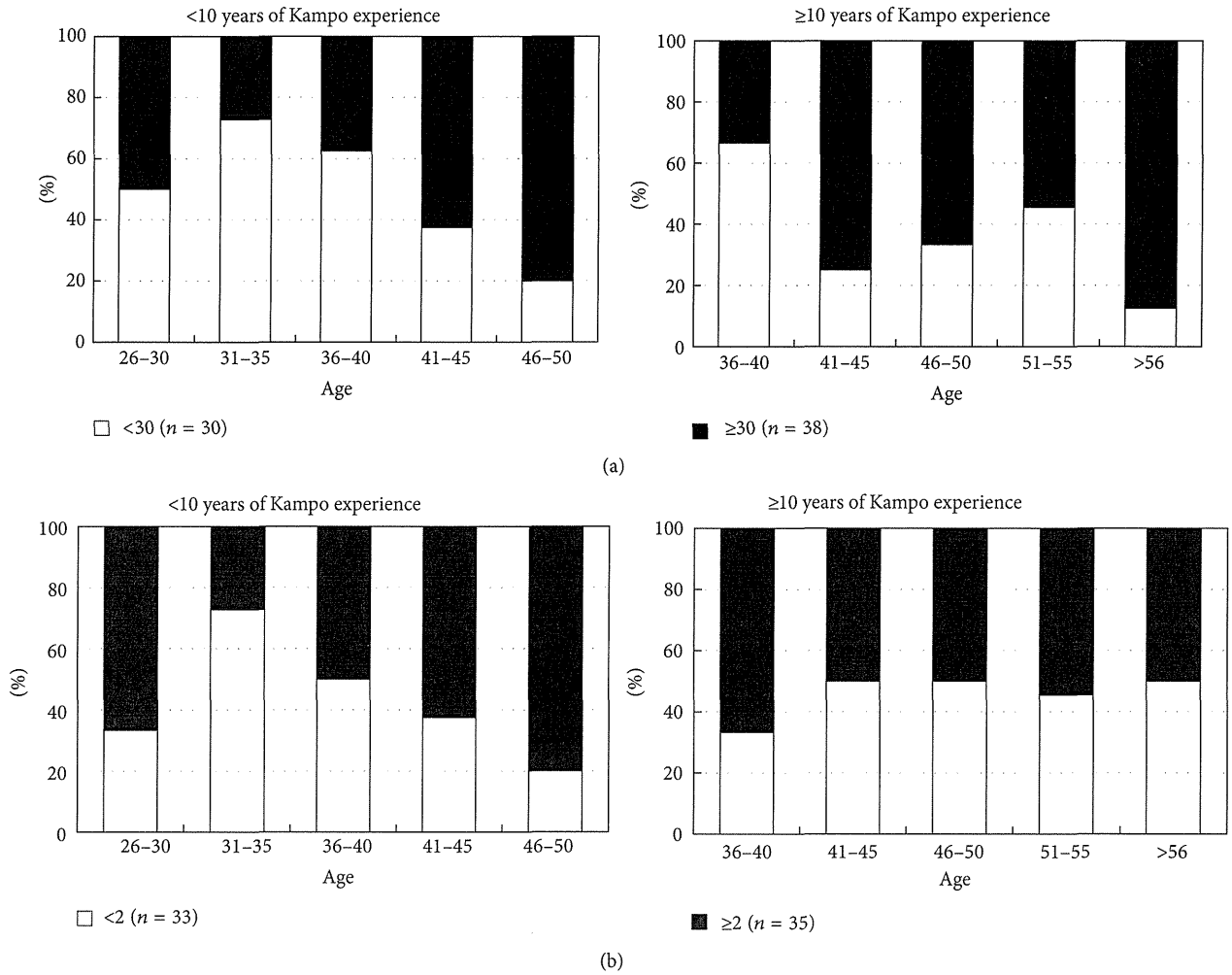

FIGURE 6: (a) The <10 years of Kampo experience group and ≥10 years of Kampo experience group were divided into EHS < 30 (n = 30) and EHS ≥ 30 (n = 38) in each age group. There was no significant relationship between Kampo experience and high/low EHS. (b) The <10 years of Kampo experience group and ≥10 years of Kampo experience group were divided into 64–78 HS < 2 (n = 33) and 64–78 HS ≥ 2 (n = 35) for each age group. A significant difference was observed in the 64–78 HS < 2 group between the <10 years and ≥10 years of experience groups (χ^2-test, $P < 0.01$). The ages were higher in the ≥10 years of Kampo experience group, but the ratio of 64–78 HS < 2 did not decrease.

by both the illumination light source and the characteristics of the object. Hence, the settings of the illumination light source, the light source position, and the observation viewpoint are important in order to obtain an accurate representation of the color. Zahiruddin et al. compared two conditions for the Hue test, the conventional observation method and observation under ambient room light. They recognized that Hue scores differed in the two conditions [24]. In order to control the conditions, we followed the method of D. Farnsworth, in which the angle of illumination was vertical at 90° and the angle of Hue test viewing was about 60° in an otherwise dark room [22]. On the other hand, the human visual system has two modes of appearance of the color; that is, the two visual characteristics are the light source color mode and the object color mode [25]. Usually, we observe tongue color in the object color mode. Therefore, in this experiment, we observed the tongue color in the object color mode using a projector. The measurement value in CIE 1976 $L*a*b*$ color space had been preset using the color caps of Hue test and the tongue color images. However, as the color is affected by the experimental environment, we also measured actual values (CIE 1976 $L*a*b*$) in the experimental environment. We set a TCR that matched the color caps of the Hue test and the tongue color images in the actual measurement value. Number 64–78 caps from the Hue test were considered equivalent to the color of tongue diagnosis. The method used to identify the red-green or blue-yellow area in the Hue test has been described in previous reports [17, 26]. In this study, different results were obtained when the data of this restricted area of color were evaluated instead of the entire area of the Hue test.

In general, it has been reported that discrimination of colors represented by the entire Hue test region worsens with aging [27–29]. Similar results were observed in this study. In Kinnear and Sahraie, the average Hue scores decreased gradually to about 20 years of age, but after 20 the scores

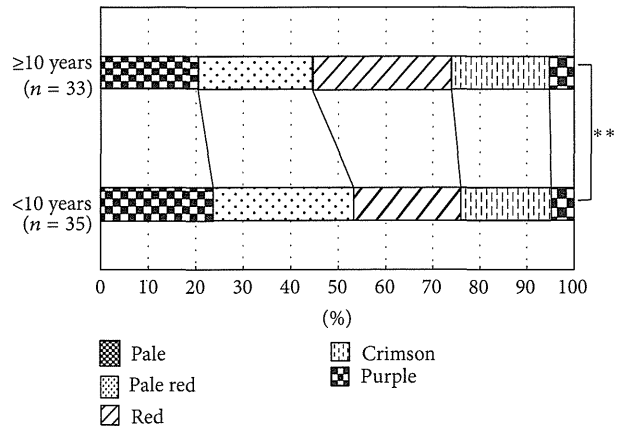

FIGURE 7: Comparison of TCD and duration of Kampo experience. The distribution of TCD showed a significant difference in the comparison of the <10 years and ≥10 years of Kampo experience groups. All P values were obtained by χ^2-test. $^*P < 0.05$,$^{**}P < 0.01$.

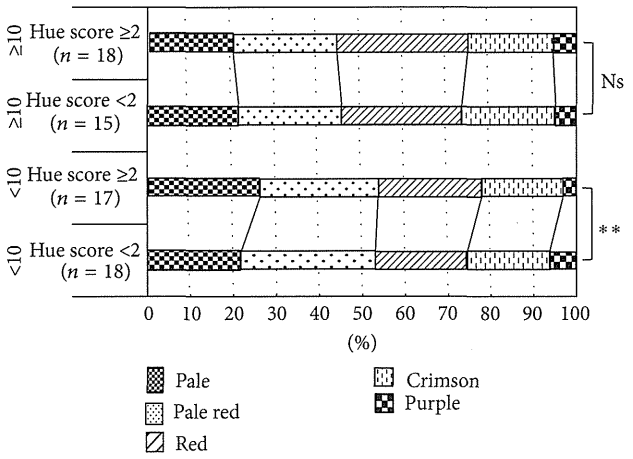

FIGURE 8: Comparison of TCD with 64–78 HS and duration of Kampo experience. The distribution of TCD was significantly different in the 64–78 HS < 2 and ≥2 groups within the <10 years of Kampo experience group. On the other hand, no significant difference was found in the ≥10 years of Kampo experience group. All P values were obtained by χ^2-test. $^*P < 0.05$, $^{**}P < 0.01$, Ns: no significance.

increased with aging (color discrimination worsened). The average Hue score was found to increase greatly at 50 years or more [27]. Roy et al. reported the same results [28, 29]. However, the average Hue scores in our study are lower than those in these previous reports. Likewise, the rate of increase of average Hue score for subject's ≥50 years in this study was lower than in these reports. We found an effect in this study whereby the color discrimination of the TCR does not suffer an age-related worsening in Kampo practitioners with ≥10 years of experience. We think this effect explains our results.

There was no significant difference in color discrimination by gender (Hue test entire region and TCR). Some reports have compared color discrimination by gender using the Hue test [26, 30]. Rigby et al. examined Hue test color discrimination by gender in pathologists [30] and found no significant difference between the scores of 23 males and 7 females in the 20–45 years age range. Moreover, Koçtekin et al. considered specific regions of Hue test in the dominant eye and the opposite side of eye of medical students [26]. The subjects were 31 males and 19 females whose mean age was 21 ± 2 years of age. Again, there was no significant difference between males and females in their study. Although the designs and purposes of these reports were different from those in this study, the results are consistent. Therefore, although the male-to-female ratio of this study was not 1 : 1, we think the effect of this bias is small.

In the TCD, no association was found between age, gender, and color discrimination (Hue test entire region and TCR). However, a significant difference in TCD was recognized between inexperienced (<10 years) and experienced (≥10 years) practitioners. Thus, an association was suggested between TCD and duration of Kampo experience. The inexperienced group tended to evaluate the pale-red area more broadly than the experienced group. Conversely, the experienced group tended to evaluate the pale and the pale-red areas more narrowly and to evaluate the red areas more broadly. Thus, there is a possibility that the ability to identify the pale-red area (normal tongue color area) is increased by gaining experience in Kampo medicine. We examined the TCD results by two factors, color discrimination of TCR and duration of Kampo experience. In the inexperienced practitioner group (<10 years), TCD results differed depending on the color discrimination of TCR. On the other hand, in the experienced group (≥10 years), TCD results were not affected by the color discrimination of TCR, but rather the TCD results became constant. Therefore, until having enough TCD, training of Kampo medicine may be needed for 10 years or more.

Actual clinical doctors diagnose tongue color independently. For this reason, we think this study is valuable because it involved the participation of many Kampo medical practitioners. Moreover, the finding that the TCD is affected by duration of Kampo experience is novel. Using this new finding, it may be possible to obtain more accurate results in the selection of tongue color diagnosis. We need to consider the duration of Kampo experience when judging tongue color findings. Further, in Kampo medicine education, age or color discrimination ability should not be considered a barrier, as experience and training can make up for these deficits. This study suggests the importance of TCD study, which we hope will progress in future. Finally, we believe this study can contribute to the standardization of tongue diagnosis in Kampo medicine.

5. Conclusions

Overall color discrimination worsened with aging, but the ability of tongue color diagnosis was not affected by aging or color discrimination ability. The ability of tongue color diagnosis and indeed ability to discern colors in the tongue color region do not degrade in those with Kampo experience. These results suggest the importance of studying tongue

color diagnosis, and they are expected to contribute to the standardization of tongue diagnosis and Kampo medical education in the future.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

Acknowledgments

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Editorial

Acupuncture and Herbal Medicine for Cancer Patients

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1. Complementary and Alternative Medicine (CAM) in Cancer Care

In recent decades, cancer treatment has made remarkable progress with targeted therapy applied on targeted subpopulation [1]. Though the life expectancy of the general population is increasing, cancer is still one of the most common causes of death worldwide [2]. The sophisticated treatments are often accompanied with increased adverse events, and the survival rate is still unsatisfactory in some cancers. In advanced or recurrent cancers, the goal of cancer treatment is often not curing the disease but prolonging survival time with good quality of life. The health-related quality of life is getting value as a cancer outcome, and the effect of early palliative care is emphasized importantly [3]. Nowadays medical information is easily accessed by patients, and most of patients are looking for treatments with less side effects and all available information to prolong survival time and to improve quality of life. Therefore, complementary and alternative medicine (CAM) for cancer is increasingly being demanded by patients, and more physicians are getting interested in the use of CAM in cancer therapies.

The use of CAM in cancer therapies differs from country to country, but up to 80% of cancer patients use some kinds of CAM to support their conventional cancer treatments [4, 5]. In Southwestern China, the prevalence of Chinese herbal medicine use is up to 53.0% during cancer treatment [6], and it seems similar to that of Hong Kong [7]. In Taiwan, up to 98% of the cancer patients use any kind of CAM [8]. In Korea, 78.5% of cancer patients use CAM [9]. A Japanese study revealed that 44.6% of cancer patients use CAM [10], while 83% of cancer patients or cancer survivors use CAM treatments in Australia [11]. An European survey in 13 countries showed 35.9% of average CAM prevalence in cancer patients (range among countries 14.8% to 73.1%) [12]. In other parts of the world similar results were obtained [13]. CAM is also used by 31–84% of children with cancer [14]. This usage of CAM for cancer is more common among educated people with better health behaviour [15, 16] as well as among women [17]. In the case of female cancers, more patients use CAM; for example, 60–80% of breast cancer patients (in comparison to 50% among cancer patients in general) and 75% of female colon cancer patients use CAM [18].

Patients mostly use CAM as a complement to their conventional therapy, not as an alternative treatment [19]. Only very few patients replace conventional treatment by alternative medicine [20]. Even though the use of CAM is a fact worldwide, the view on CAM varies enormously, and the integration of CAM therapies into conventional therapies is extremely complicated in different countries.

Although the governmental support on the research on CAM for cancer therapies differs among various countries, the use of CAM for cancer patients is still debated in an ideological way by supporters and opponents of CAM. One of the causes for the reluctance of Western academia towards CAM is still the insufficient number of convincing clinical studies providing evidence for the efficacy and safety of CAM therapies. The Western concept of "evidence-based

medicine" does only poorly match to the clinical practice of CAM. Nevertheless, an increasing number of clinical studies are being conducted during the past years to gain credibility and reputation of CAM. Illustrative examples on the power of CAM have been documented in cancer research with a focus on three major fields [21]:

(i) acupuncture is widely applied for treating pain, a prominent side effect encountered during cancer therapy;

(ii) reduction of severe adverse effects of standard chemotherapy;

(iii) unwanted interactions of standard therapy with herbal medicines.

Another reason for critical opinions towards CAM regards the quality of herbal products according to international quality standards [22].

Therefore, an important question for recognition and implementation of CAM into general medical practice concerns the clinical evidence for efficacy and safety of CAM treatments.

This induces confusion and fear in patients and provides a burden for the communication between patient and doctor. Only 2.4% of patients used their healthcare professional record as primary source of information on CAM in cancer care [23] and 92% of American breast cancer patients withheld information about the CAM treatment from their medical oncologists [24]. Similar results were found in a survey in Taiwan, where more than two out of three cancer patients never informed their physicians of their CAM use [8]. Reasons for this might be the expected inflexibility of medical oncologists and patients' fear of harming the relationship with their oncologists caused by the use of CAM. It is not common for patients to have a communication between Western medicine-oriented doctors and CAM practitioners in clinical practice. However, the integrative cancer care is increasingly required by patients and recently it is getting popular in cancer treatment.

2. Acupuncture and Herbal Medicine for Cancer Patients

Acupuncture and herbal medicine are the most qualified CAM treatments. Their effectiveness is still under debate, although they have been used in many fields of cancer treatment and palliative care [25, 26]. The efficacy of the acupuncture and herbal treatment is not currently well recognized by the Western academia and clinical scholars, so that advantages of these therapies in treating cancer or supporting cancer treatment are not adequately reflected. One reason of this estimation is because of the quality of clinical research. Many studies still have the level of case studies [27], which seem like an anecdotal, and the generalization of CAM results might be questionable for scholars who are familiar with well-designed clinical trials.

Acupuncture and herbal medicine have been used for the treatment of cancer pain [25, 26] and for attenuation of side effects of cancer treatments. Acupuncture has been shown to be effective for chemotherapy-induced nausea and vomiting [28], as well as acupressure [29] and herbal medicine [30]. However, acupuncture has not been systematically evaluated with well-designed clinical trial for its effect on it, while new drugs got approvals from FDA for the relief of chemotherapy-induced nausea. Other studies showed an effect of acupuncture on xerostomia after radiation therapy [31, 32]. There are reports that acupuncture was effective on the chemotherapy-induced peripheral neuropathy [33] and herbal medicine was effective on the oral stomatitis [34], which lead patients to higher acceptance of Western cancer treatment with less interruption or discontinuation of therapy. Many studies were focused on the relief of cancer-related symptoms such as fatigue [35–37] and the improvement of quality of life [38].

Recently, randomized controlled trials (RCTs) have been conducted to seek evidences on acupuncture and herbal medicine [39–41]. These therapies are usually considered as supportive for major treatment, in order to attenuate side effects of surgery, radiotherapy, and chemotherapy.

One of the issues of RCTs on acupuncture and herbal medicine is how to deal with the individualized approach of treatments based on the Asian tradition. Asian herbal therapy is commonly a combination of multiple herbs; sometimes approximately up to 15 herbs are in one prescription, while a single herb already contains multiple tentative active compounds. The daily practice in acupuncture and herbal medicine with its individualized approach cannot be easily transferred into standardized controlled trials. The conclusion of systematic review studies that better qualified studies are necessary [42–44] is not so surprising. The study design to solve these issues should be developed.

Even though the effects of acupuncture and herbal medicine are still under debate and further clinical research is necessary, the clinical use of acupuncture and herbal medicine has already been recommended to control cancer-related symptoms in some of the clinical practice guidelines. According to the evidence-based guidelines of the *American College of Chest Physicians for Lung Cancer*, acupuncture has been recommended as a complementary therapy for lung cancer when pain is poorly controlled or when side effects such as neuropathy or xerostomia are clinically significant [45].

Acupuncture and herbal treatment have been used as a complementary treatment in combination with highly effective and partly aggressive Western medicine such as chemotherapy or hormonal therapy. But interactions are quite unknown, underestimated, or under debate. For instance, the herbal treatment with hormone-active herbs in patients with hormone-sensitive cells of breast or ovarian cancers is an important topic of ongoing debates [46, 47]. The interaction of acupuncture and especially herbal medicine with conventional treatments is not all known. Guidance on the safety of herbal medicine to prevent potential risks to cancer patients is necessary, but data have not yet been collected systematically in Mainland China but are now being established in Hong Kong.

In Japan, Kampo, traditional Japanese medicine, is extensively used for cancer patients as supportive measures, covered by National Health Insurance. Japanese medical doctors

can prescribe both Western and Kampo drugs, knowing the natural history of diseases and the indication and limitation of Kampo. But, there are no strong recommendations on the Kampo use based on high-quality evidence in clinical practice guidelines in Japan [48]. The Japanese medical system is a unitary one, and Kampo is practiced in this system. From this point of view, the system of Japanese traditional medicine is different from those of China and Korea, where traditional medicine is generally practiced in a dual system, but in the recent years integrative approaches were developed. Japanese Kampo practitioners take advantage of this unitary system, conducting high-quality clinical practice and research. This situation consequently leads to the integrative medicine by a single doctor, whereas the integrative medicine in other countries is usually done by a Western medicine doctor and a traditional medicine practitioner. The system of Japanese Kampo medicine well fits the methodologies of modern medicine, and many clinicians utilize Kampo, accumulating evidence data. This unified situation might be an inspiring example for countries with a unitary medical system.

In Korea, the government health insurance covers only acupuncture treatment for cancer patients. In Western countries, acupuncture and herbal medicine, in spite of frequent use, for years were not in the main focus of the medical academic society. So, research in this field was limited leading in consequence to a situation that especially treatments with Asian herbs often had a lack of scientific controls. But due to increasing interest of patients and practitioners, acupuncture had partly become an integrative therapy in pain management, and, for example, in Germany the use of Western herbs as a complementary medicine is common and Asian herbs are increasingly used.

Since herbal therapy is the most commonly used CAM treatment [49], in recent years, the search for active compounds has mainly focused on Asian herbs, whereby the emphasis has been on classical product-based leads for Western drug discovery, usually performed by screening the extracts or compounds from diverse biological sources. Many *in vivo* experiments showed effectiveness on cell cultures and in animal models [50–53], but translation from bench to bedside is still a difficult challenge. This research, mainly focusing on single active compound, has been done often without regard to preexisting knowledge of the therapeutic utility of the plant source [54]. While interactions of ingredients during the preparation procedure are sometimes essential to the therapy, an extraction of the active ingredients is often not a simple task, and evidence shows that single components extracted from plants are less potent than the crude extract [55]. Scientists of many countries worldwide have tried to apply modern experiment-based research methods to isolating active compounds from herbs, characterizing their pharmacodynamic and pharmacokinetic properties and defining their molecular modes of action with limited success. This reductionist paradigm of a "single chemical entity" is not easily applicable to the multidimensional complexity of Asian herbal prescriptions. Researchers often do not use any concepts of traditional theory as the basis for their investigations on these compounds [56].

Studies on the influence of single herbs or their components on different microbiological pathways of human physiology are necessary and important, but this research is not likely to lead to single-component treatments for multifactorial diseases such as cancer. Cancer is a systemic disease of the entire body. A single-target approach has limited effectiveness, and there is evidence that a multitarget approach might be more effective [57, 58]. It seems only rational to apply a multitargeted therapy to a multifactorial disease. The realization that multicomponent medicines may have advantages over single-component drugs has a scientific foundation. The pharmacological advantages of mixtures may lie in the potentiating action of their multiple bioactive components and the advancement of individualized therapy [59, 60].

Modern research methods on a single herb aimed at isolating active compounds from herb have to be the fundament for future researches in herbal medicine. But when basic information is found and made available, experiments with herbal combinations might be the productive direction for further research to control cancer. While cancer is a multifactorial disease with diverse heterogeneous mechanisms, a combination of components might provide a promising opportunity to focus on multiple targets. Furthermore, these efforts may eventually offer an individualized approach to the treatment. Basic research on single herbs and their active compounds is still essential for the scientific understanding of traditional herbal medicine. But research should not stop at this level but continue with research on multicompounds, their interactions, and increasing or decreasing activity in combinations. Gaining knowledge from tradition might be helpful, not ending in a dead end. This approach is ambitious and time-consuming but has a chance not to fail like conventional drug discovery procedure in the field of herbal medicine in recent years.

While it is difficult to get a patent on natural products, the further interest of pharmaceutical companies might be limited. Progress in this research area can only be found in intense national as well as international cooperation, founding international joint working groups to overcome the obstacles of this sophisticated challenge.

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