特　集

CoSTR 2010 に向けて

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ILCOR 2009 の日本開催がきまる

CoSTR（Consensus on CPR and ECC Science with Treatment Recommendations）2010 は 2005 版から新たに改訂されることになったのは既に説明した．2007 年から春，秋の年 2 回の開催となり，2007 春は南アフリカ，秋は Orlando で開催された．この秋の 11 月 1 日，2 日の ILCOR 会議で 2010CoSTR 作成のための Road Map/Timeline が決まった（**図1**）．JRC はアジアをまとめて RCA（Resuscitation Council of Asia）を立ち上げ，7 番目の ILCOR 加入となったのが 2006 年であった．ILCOR 開催の Road Map で2009 年春の開催地が未定であって，これがどこに決まるかが JRC にとり最大の関心事であった．

ブラジルが 2003 年に Recife（ブラジルのリゾート地）で開催した．サンパウロから 2000 キロの距離での開催であったが，ブラジルの厚生大臣が開会式に出席して祝辞を述べるという熱意を国を挙げて示した．それが契機になり中南米の蘇生学が進展したのを見ていたので，2010 の前の年の 2009 年に日本で ILCOR 会議を開催できると，①日本でほとんど知られていない ILCOR の存在と活動を周知できるだけでなく，②日本国内の各学会からの evidence を発信する動機づけになり，③アジア諸国での蘇生学と蘇生 training の飛躍的発展が期待でき，④CoSTR2010 から ILCOR の正式メンバーとしてAHA，ERC と同時に ILCOR の情報が手に入り，独自に日本版またはアジア版ガイドラインが作成できるなどの merit が期待できる．このような点でアジアに招致できればと思い，2009 春の開催地として手を上げた．

ILCOR は各地域の代表の集まりで運営されているが，AHA 7 名，ERC 7 名，ANRC（オーストリア，ニュージーランド蘇生委員会）3 名，カナダ（HSFC）2 名，南アフリカ（SARC）3 名，南アメリカ 1 名，アジア蘇生協議会 3 名による投票で開催地が決まる．立候補したカナダとアジアとの競争になったが，2009 年春の開催地としてアジアが ILCOR Business Meeting で決定された．

筆者は 2000 年から ILCOR にオブザーバーとして出かけていて，2006 年に正式メンバーになるまで毎回出席したその熱意も買われたのかと胸が熱くなった．この presentation を畑中先生に行ってもらったが，流暢な英語で説得できる話し方をしてもらった．

Road Map のように worksheet の次々の完成が主な作業になるが，年 2 回の開催となり，秋はアメリカで開かれるが，2008 年春は Ghent で開催され worksheet が全体の 25%が作成され，2008 年秋の New Orleans で 60%が完成され，2009 年春の日本（大阪）で 100%の worksheet が完成されることになる（**図1**）．

アジアから，日本からの evidence を示して 2009 の日本開催による成果をぜひ 2010CoSTR に反映したいと願っている．日本循環器学会が笠貫心肺蘇生委員会委員長の絶大な御尽力により，日本循環器学会の前々日，その前の日の 2 日にわたり大阪で開催する具体的プランを Orlando で説明でき，おかげで ILCOR の日本開催が決定され日本循環器学会および笠貫教授はじめ循環器学会理事のご好意を心から有難く思っている．学会前日には ILCOR の各地域の代表による International Resuscitation Science Symposium が設けられる予定になっている．雑誌でしか名前を知らない expert の参加する豪勢な Symposium は国内の蘇生学の学際的発展にもよい刺激になると思う．

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表1(1)　Orlando の ILCOR 会議の日程表

International Liaison Committee on Resuscitation
ILCOR

ILCOR Meeting Agenda
November 1-2, 2007
Rosen Centre Hotel, Orlando, Florida

- Wireless Network Name for meeting rooms is ILCOR.
- Staff Office is Suite 235

Thursday, November 1

Room: Salon 1-2 Foyer
6:30-5:00 **Registration**

Room: Salon 5
6:30– 7:45 **C2010 Steering Committee and Task Force Co-Chairs Breakfast Meeting**
Breakfast will be served. Discussion will begin at 6:30AM.

Room: Salon 1-2
7:00-7:45 **C2010 Delegate and Task Force Member Breakfast**

Room: Salon 1-2
8:00-10:00 **I. Plenary Session I**

A. Opening Remarks, ILCOR Mission and Introductions — **Vinay Nadkarni/Jerry Nolan**

B. Road Map to C2010 — **David Zideman/Robert Hickey**

- Timeline for future meetings and worksheet completion
- Fall 2009 "Goal" of initial evidence evaluation conference
- February 2010

C. Feedback on the Worksheet process

- Educational session on evidence evaluation process including:
  - Non-intervention: worksheets
  - Assignment of "Quality of Evidence"
  - Identification of questions (incl. Global Evidence Mapping)
  - Presentation of Work Sheet Reviews to entire group for general discussion.
    - Feedback – Peter Morley
    - Hypothermia – Jerry Nolan
    - Prognosis – Arno Zaritsky

Room: Salon 1-2 Foyer
10:00-10:15 **Refreshment Break**

表1(2) Orlando の ILCOR 会議の日程表

Room: Assignments Below
10:15-11:45 II. Task Force Breakouts
- **A. ACS MI - *Room: Salon 23***
- **B. ALS - *Room: Salon 6***
- **C. BLS – *Room: 8***
- **D. Education/Implementation/Teams – *Room: Salon 5***
- **E. PLS – *Room: Salon 7***

Each task force begins by presenting one worksheet with discussion of how the Evidence Evaluation process and tools fit their task force work needs, followed by:
- Accept/reject questions and finish triaging questions into Retire/Update/New category
- Identify new questions using Global Evidence Map
- Prioritize questions according to road map
  - Discussion of Road Map to C2010
- Begin to assign worksheet authors, if possible

Room: Salon 1-2
12:00-1:00 Lunch (Non-Delegate Task Force Members)

Room: Salon 9
12:00-2:30 Lunch and ILCOR Business Meeting (Delegate Only)

Room: Assignments Below
1:00-4:30 III. Task Force Breakouts (cont.)
- **A. ACS MI - *Room: Salon 23***
- **B. ALS - *Room: Salon 6***
- **C. BLS – *Room: Salon 8***
- **D. Education/Implementation/Teams – *Room: Salon 5***
- **E. PLS – *Room: Salon 7***

Continue from morning breakout session as well as individual task force worksheet presentations. (ILCOR delegates will rejoin task forces at 2:45pm after business meeting ends.)

Room: Salon 1-2 Foyer
3:00-3:15 Refreshment Break

Room: Salon 1-2
4:30-5:30 IV. Plenary Session II
- **A. Debrief from day one** — **Peter Morley**
- **B. Announce Spring 2009 Site Selection** — **Jerry Nolan/Vinay Nadkarni**
- **C. Are we on Track?**
- **D. Problems with PICO?**
- **E. Acceptance of road map to C2010**

Room: Salon 5
5:40-6:00 V. C2010 Steering Committee Debrief

6:30-9:00 Offsite Dinner – Adventurers Club, Pleasure Island (Cash bar will be available.)
Buses will depart the Rosen Centre at 6:30PM.

At the Adventurers Club you can expect outrageous entertainment as the world's most eccentric explorers welcome you to their legendary club of the 1930's. Swap tall tales with a marvelously mad professor and other characters while you enjoy live shows featuring everything from talking masks and a floating head to a ghostly piano!

表1(3)　Orlando の ILCOR 会議の日程表

Friday, November 2

Room: Salon 5
6:30– 7:45　**C2010 Steering Committee and Task Force Co-Chairs Breakfast Meeting**
Breakfast will be served. Discussion will begin at 6:30AM.

Room: Salon 1-2
7:00-7:45　**C2010 Delegate and Task Force Member Breakfast**

Room: Salon 1-2
8:00-9:30　VI. **Plenary Session III**
A. Non-Intervention Worksheet Presentations (Diagnosis:ACS) — **Judith Finn**
B. Discussion of unresolved worksheet and process issues — **Peter Morley**
- Feedback from Day 1
- Merging or separate - Dr. Nolan and Ms. Hazinski
- Sharing questions across Task Forces
- Continued discussion of road map to C2010

Room: Salon 1-2 Foyer
9:30-9:45　**Refreshment Break**

Room: Assignments Below
9:45-11:45　VII. **Task Force Breakouts**
A. ACS MI - *Room: Salon 23*
B. ALS - *Room: Salon 6*
C. BLS – *Room: 8*
D. Education/Implementation/Teams – *Room: Salon 5*
E. PLS – *Room: Salon 7*
- Presentation of worksheets
- Accept/reject questions and finish triage into Retire/Update/New categories
- Identify new questions using Global Evidence Map
- Prioritize topics/worksheets for Ghent (next ILCOR meeting) and assign worksheet authors/presenters

Room: Salon 1-2
12:00-1:00　VIII. **Plenary Session IV – Working Lunch**
A. Timetable for future meetings
B. Other business

Room: Assignments Below
1:00-3:00　IX. **Task Force Breakouts (cont.)**
A. ACS MI - *Room: Salon 23*
B. ALS - *Room: Salon 6*
C. BLS – *Room: 8*
D. Education/Implementation/Teams – *Room: Salon 5*
E. PLS – *Room: Salon 7*
- Review worksheets
- Discuss worksheets and plan for merging evidence evaluation Summaries and treatment recommendation sections
- Future plans for working as a task force
- Assignment of prioritized worksheets for Ghent

Room: Salon 1-2
3:00-4:00　X. **Plenary Session V** — **Jerry Nolan/Vinay Nadkarni/David Zideman/Robert Hickey**
A. Review of Road Map to C2010 and Task Force Roles and Responsibilities
B. Meeting Summary
C. Task Force Feedback
D. Plans for Next Steps
E. Ghent Meeting Plans — **David Zideman**

Room: Salon 5
4:10-5:00　XI. **C2010 Steering Committee Debrief**

Worksheet 作成作業

Orlando の ILCOR 会議は ILCOR Business Meeting に続いて 2 日間にわたり worksheet の作成に関して熱心に討議された（**表1**）.

2005 の ILCOR の作成した Document は CoSTR (Consensus on CPR and ECC Science with Treatment Recommendations) と呼び，2010 も世界中でガイドラインを各国が作る基本にする立場から CoSTR の作成をより充実することになった．したがって蘇生に関する文献を網羅すべく検索を徹底することから始まり，最新の情報を集める検索網を 2005 のときより発展させた．世界の数百人の expert に参加してもらい，蘇生の範囲を予防から post-resuscitation care まで広めた．Worksheet の主題も治療法，診断手技，予後指標に関するまで広げ，さらに CPR 教育，training に関する主題も取り上げた．Education/ Implementation Task Force が取り上げられているのはそのためである．年齢も新生児，小児から老人までを網羅した Task Force が組まれている．Worksheet は 2005 で利用した template を改良してより客観性を持たせて，この review process もスピードアップするようにした．この世界中から集積した文献は無差別比較対照試験から症例報告，動物実験，モデル研究までも集め，英語だけでなく異なった言語の文献も集めるようにした．RCA が加入したのはアジアからの evidence を発信するよい機会であるし，CoSTR がより global 的になるのに貢献できる．

さらに蘇生の救命率が低い現状から 2010 を超えてより長い span での継続性が強調されている点も重要である．

2010 に向けての worksheet の作成について解説する．Worksheet を 3 部で構成する戦略が以下のように立てられた．

1) 2005 年での未解決な問題点は積み残しの主題なので GAPS TOPICS として枠が設けられた．

2) 2005 年で取り上げられた Topics を 2010 で再度取り上げるか，棄却するかの選択も再評価という形で進められた．

3) 2010 に向けての新たな Topics を new の分類で取り上げる作業が 2005 以降の evidence の集約に基づき始まった．

今回から Evidence Evaluation Expert (E3) としてオーストラリアの Peter Morley が指名され，リード役となったため 2005 のときと比べて worksheet の作成の手順がかなり円滑に進んでいる．

表1[1] に Orlando での ILCOR の agenda を示すが，11 月 1 日，2 日と忙しい予定が組まれていた．Plenary lecture に続いて，BLS，ALS，PALS，ACS の Task Force に分かれて Ghent で討議して完成する worksheet を優先順位をつけて選ぶ検討がなされた．First Aid，Neonatal，Stroke の分科会は今回は開かれなかった．

Peter Morley が E3 (Evidence Evaluation Expert) として会全体の進行を行ったが，Orlando 30:2 と示した問題点を**図2** のように示した[1]．この図の上段から意識の確認の best sign は？ 初回に施す呼吸の回数は？ 胸骨圧迫と呼吸の比率は？ Sign of life? (2005 での循環のサイン)，AED の energy level，waveform？ AED の直後に CPR は何分行うか？ このときの気道確保法は？ 呼吸回数と 1 回換気量は？ 昇圧薬とその投与時期は？ ALS になるが 5 個の H と 5 個の T の原因での症候と新たな対策？ 薬物治療として，ことに抗不整脈薬の選択？ などが討議の対象になる大筋が示されている．

ILCOR 構成の Council に対して 2005 の worksheet author とは別に 2010 のために up date された worksheet 作成への参加を各 Task Force が呼びかけていた．RCA から正式に BLS に韓国，ALS にシンガポール，Implementation に台湾，PALS に日本，Neonatal に日本，Stroke に日本から各 author を推薦した．さらに author をとの求めで日本から BLS，ACS/AMI，台湾から BLS に新たに最近推薦したが，Ghent での作業が迫ったためであろう．

Scientific Knowledge Gaps[2]

2005G の作成で 2000 以降の CPR に関する科学的論文で明確な回答が得られずに積み残しになっていたのがあった．

2010G に取り上げる場合にこの Topics を優先して検討することにした．すなわち 2005 での 276 の Topics を再度取り上げて，Scientific Knowledge Gaps となづけた枠を設定した．2005G では 276 の Topics が示され各 Council worksheet author が 281 人参加して 1 題に 2 人が関わり，403 の worksheet

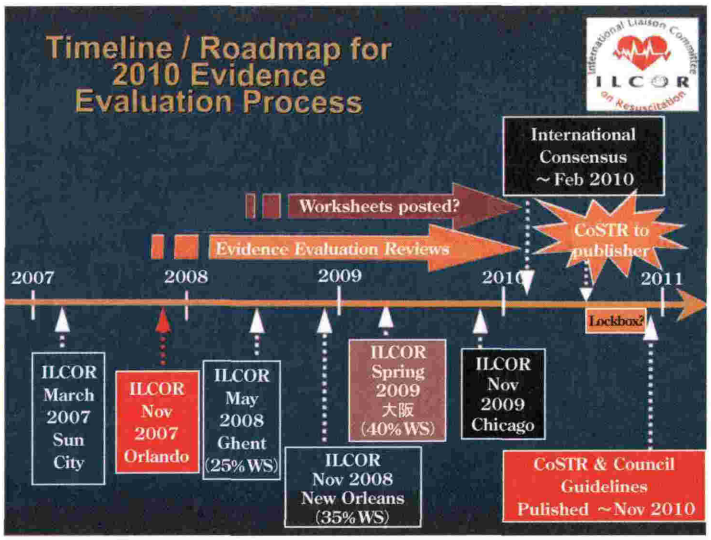

図1　CoSTR の作成過程
（2009 年は大阪で開催）

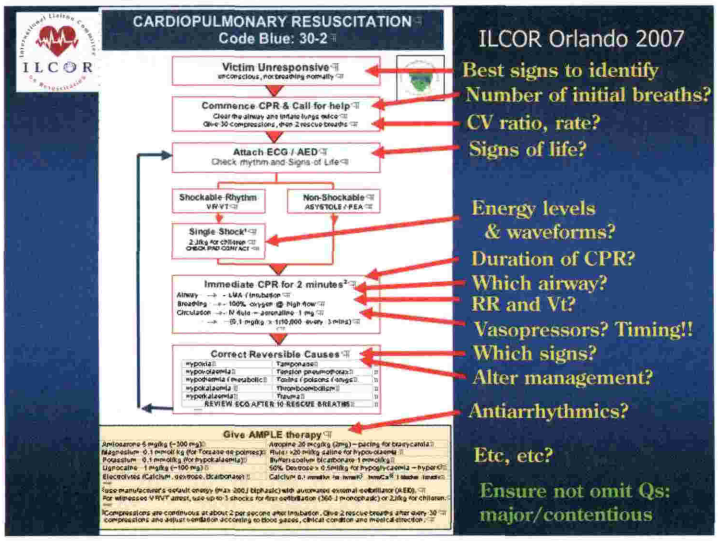

図2　CPR：Code Blue 30:2 での討論会
（Peter Morley）

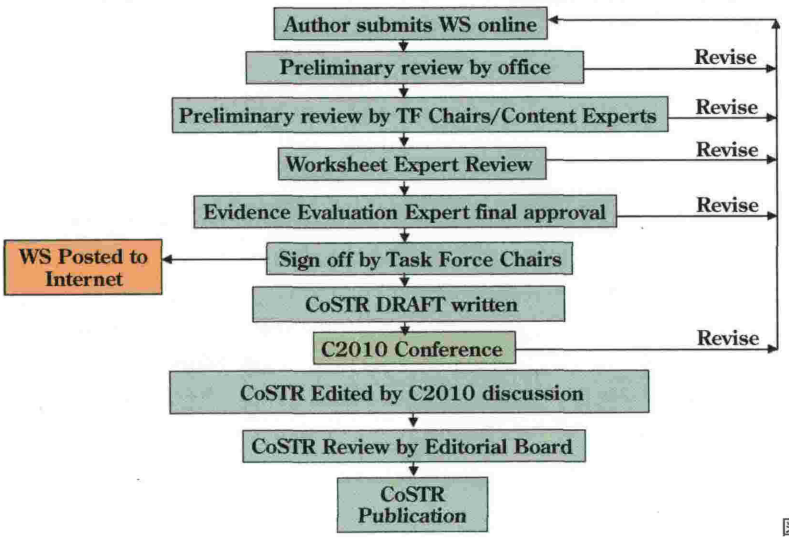

図3　C2010 Worksheet Flow Draft

を作成した．そして最終的に2010GのGapsとして199の主題が決定された．これを，①Resuscitation，②Acute Coronary Syndrome，③Stroke，④First Aid，のカテゴリーに分類して，各Task Forceが個々の分野から優先して取り上げるTopicsを10〜15題選ぶことになった．

心停止の治療でのevidenceは中枢神経の後遺症がなく生存退院するのがLevel 1 Evidenceの評価となり，Class 1のRecommendationになる．ACS，Stroke，First Aidでは病状の改善，全身機能が保持されてる状況で判断している．

以下の**表2**〜**4**にGaps Topicsを示す．**表2**にResuscitationでの優先検討の順位を選ぶTopicsを示す．成人，小児，新生児をまとめてTopicsを選ぶ作業がなされたが，成人，小児と分類するとoverlapが目立つので，まとめて蘇生としての枠で次のように区分けした．

1. Medical Emergency Teams，2. Recognition of Cardiac Arrest and its Causes，3. Body Position，4. Electrical Defibrillation，5. Blood Flow Generation，6. Airway Management，7. Ventilation，8. Oxygenation，9. Pharmacological Intervention，10. Metabolic，Temperature，and Post Resuscitation Management，11. Physiological Monitoring，and Post Resuscitation Management，12. Ethical Issues，13. Education and Training，14. Outcomes

2.の心停止ではこれを早く発見して，その原因をすばやく探せる点を検索する．3.の体位は気道確保との関連で，特に頚椎損傷時を取り上げる．4.の除細動では波形の適正とは？ 除細動の前と施行中の胸骨圧迫はどのようにするか？ 除細動後の心機能は短期，長期的に障害されないか？ Public Access DefibrillationやHome AEDの意義，最初の発見者による除細動の効果などが検討される．5.のBlood Flow Generationは2010Gで最重要な部分であるが，compression-only CPRが有効か？用手胸骨圧迫と器具によるのでどちらがよい効果が得られるか？胸骨圧迫の質の改善が最重要である点が強調されている．

Airway Impedance Threshold Deviceの循環維持への効果，胸骨圧迫中断時間を最小にするように蘇生のほかの手技（人工呼吸，AED操作）を工夫する．6.の気道確保では上気道確保法，Bag-Mask法と高規格気道確保法での換気の行いやすさ，Combi Tube，気管挿管が気管に確実に入っているかの確認，気道確保の訓練法は？ 7.の換気では年齢に応じてcompression-ventilation比と換気量は？ 換気が多すぎるときに，real-timeに調整して，循環への悪影響を少なくする装置の導入．8.の酸素供給に関してでBLSで蘇生に必要な酸素量は？新生児では空気での蘇生は？ など．

9.は薬物についてのTopicsで昇圧薬，抗不整脈薬，アトロピンでevidenceで生存率が高まるとのデータが不足している点の解明が求められる．

ベーターブロッカーはselectivity，duration of actionが，さらに新しい昇圧薬，再還流障害の対策としてミトコンドリアATP-sensitive K Channel Openerなどが取り上げられている．これらの投与ルートと投与時期の検討も求められている．

10.ではPost Resuscitation Managementで低体温の有効性，この実施法の実地面での検討，血糖値の管理，Post-Resuscitation Phaseでの循環作動薬の適応？ 11.では最近注目されている心蘇生中，後でのreal-time monitoringがいかにあるべきか？14.のOutcomeでは心停止の生存者でQuality of Life，長期生存成績が検討されるよう求められている．

表3にACS/AMIの優先順が詳しく説明されているので示す．

ACSでの優先は“Prehospital and Emergency Department Assessment”，“Antiplatelet Drugs”，“Heparin”，“Beta Adrenergic Blockers”，“Reperfusion Strategies”である．Prehospital Assessmentでは12誘導ECGのST Segment上昇患者での応用の検討，ベーターブロッカーのPrehospital useは？ など

表4ではStrokeでの優先順位が示されている．“Stroke Center”，“Pharmacological Interventions”，“Metabolic Management”，“Neuroprotective Therapies”，“Transient Ischemic Attack”，“Intracerebral hemorrhage”が検討される．

First AidはAHAのworksheetにのみあげられているが，“Bleeding”，“Joint Injury”，“Skin Burns”，“Bone Fracture”，“Spinal Injury”，“Local Cold Injury”，“Snake Bite”，“Oral Poisoning”，“Allergic Reaction”，“Oxygenation”が優先課題になっている．

このKnowledge Gapsを2010 CoSTRで優先する

ためにこれまでの文献集積，多施設無作為臨床trial，新しい手技の導入とその臨床評価が求められる．これを進めるために学際的な“Pulse Initiative”(Post-resuscitative and initial utility in life saving effort) Conference がワシントン郊外で AHA が支援して開催されたが，その成果は蘇生科学での手技，モニターについての基礎的データの蓄積となった[3)4)]．さらに臨床ベースでのデータを蓄積するためにResuscitation Outcomes Consortiums を 11 の施設をあつめて立ち上げた．

2010 CoSTR の作成はこの積み残しともいえる貴重な Topics がまずとりあげられる．

表2 Research Priorities in Resuscitation of Adults, Children, and Neonates

Medical Emergency Teams

・**Do medical emergency teams (also known as rapid response teams in the United States) reduce the incidence of in-hospital adult and pediatric cardiac arrest and improve outcomes?** Evaluate optimal personnel composition and proper triggers for team activation/consultation (eg, early warning scoring systems). For pediatric resuscitation, compare informal versus formal medical emergency teams and determine the effectiveness of scoring systems for proper team response.

Recognition of Cardiac Arrest and Its Causes

・**Do techniques for establishing the presence, cause, and mechanisms of arrest (eg, cardiac versus asphyxial arrest) help tailor the resuscitation effort and improve outcome?** Determine reliable methods of establishing the presence of cardiac arrest and the need for resuscitation (eg, failure to respond to rescuers, presence/absence of signs of breathing). Consider methods to differentiate gasping (agonal breathing) from normal breathing and methods or devices to detect the presence (or absence) of cardiac activity. Identify effects of position (eg, face down) and presence of neck injury.

Body Position

・**What are optimal body positions during and after resuscitation?** Investigate methods to secure airway patency and avoid spinal cord injury. Define alternative positions for resuscitation on the basis of the victim's age, rescuer's skills, cause of arrest (eg, trauma, drowning, intoxication, arrhythmia, or asphyxia), and recovery.

Electrical Defibrillation

・**Do specific strategies for delivery of electrical shocks influence outcome?** Determine optimal energy level of initial shock (eg, 120, 150, 200, or 360 J) and of subsequent shocks (eg, fixed versus escalating). Determine optimal duration of CPR between defibrillation attempts. Determine optimal electrode position.

・**Does a period of chest compression before delivery of electrical shocks improve outcome?** Evaluate effects of duration of untreated cardiac arrest, witness status, bystander CPR, duration and quality of CPR, whether arrest occurs in the hospital or out of the hospital, and use of manual or automated defibrillation on patient outcome. Determine whether real-time VF wave form analysis may help identify optimal timing for delivery of electrical shocks.

・**What are the effects of electrical shocks on short-and long-term myocardial function?** Are electrical shocks detrimental to the ischemic heart? Assess these effects, particularly in the pediatric population.

・**What are the safety and efficacy of home defibrillation, public access defibrillation, and defibrillation by first responders?** Determine optimal AED algorithm (eg, single versus stacked shocks) and energy level of initial and subsequent shocks. Assess impact of added AED capability for monitoring and guiding the resuscitation effort.

Blood Flow Generation

・**What are the safety and efficacy of compression-only CPR?** Identify settings that may benefit from compression-only CPR; consider the cause of cardiac arrest, airway patency, gas exchange coincident with chest compression, and presence of agonal breathing. Define duration for safe suspension of ventilation.

・**What are optimal compression depth, compression rate, duty cycle, and hand position during manual CPR?** Determine optimal compression timing, compression depth, compression rate, and duty cycle in relationship to hand position by measuring blood flow generation and outcomes after manual CPR. Consider factors such as age,

gender, and body type of victims and rescuers, as well as ability to teach, learn, and retain skills.

・**What are the safety and efficacy of alternative closed-chest manual CPR techniques?** Investigate whether techniques such as high-frequency CPR, active compression-decompression CPR, phased thoracic-abdominal compression-decompression CPR, and interposed abdominal compression CPR improve resuscitation outcomes compared with standard manual CPR. Identify optimal compression rate, depth, duty cycle, time interval between components, and influence of mechanism of arrest (eg, cardiac versus asphyxial arrest).

・**What are the safety and efficacy of automated mechanical CPR techniques?** Consider compression techniques based on piston devices and load-distributing bands. Define optimal compression rate, depth, duty cycle, and influence of mechanism of arrest (eg, cardiac versus asphyxial arrest).

・**Do airway impedance threshold devices improve outcome from cardiac arrest and other low-flow states?** Consider safety and efficacy in relation to various resuscitation techniques.

・**Do interruptions in chest compression prompted by other CPR interventions compromise outcome?** Determine strategies to successfully incorporate the various ACLS tasks, such as airway management, vascular access, drug administration, rhythm analysis, and defibrillation, into resuscitation while minimizing hands-off time during chest compressions.

Airway Management

・**Do specific methods and adjuncts foster superior airway patency and ventilation?** Determine the effectiveness of methods for opening the airway, removing foreign bodies (eg, chest compression, finger sweep, abdominal thrust, chest thrust, and backslaps), and securing airway patency. Compare supraglottic airway devices with bag-mask devices or endotracheal intubation. For neonatal resuscitation, consider whether chest compression may interfere with effective ventilation, whether emergency medications and surfactant can be delivered and meconium suctioned, and whether placement of an LMA can be taught (eg, are airway management skills retained longer than endotracheal intubation skills?).

・**Can CO_2 detectors or other devices reliably confirm correct placement of endotracheal tubes and monitor stability during transport?** Consider various CO_2 analyzers and esophageal detection devices.

Ventilation

・**What is the optimal compression-to-ventilation ratio during CPR?** Consider mechanisms of arrest (eg, cardiac versus asphyxial arrest) and age of the victim (eg, 30:2, 15:2, or 5:1 ratio for pediatric resuscitation). Determine indications for interrupting ventilation during CPR and duration of such interruptions.

・**What are the optimal tidal volumes and respiratory frequency?** Determine hemodynamic effects of changes in intrathoracic pressure in relation to tidal volume, frequency, and duration of each breath. Consider the effects of cardiac arrest origin (eg, cardiac versus asphyxial arrest), presence of airway disease (eg, asthma or emphysema), and age of the victim.

・**What is the optimal ventilatory strategy for neonatal resuscitation in the delivery room?** Consider airway pressures, inspiratory times, devices, timing, volumes in relation to gestational age (eg, term versus preterm neonates), mechanical versus manual, PEEP, and CPAP (eg, mask, nasal mask, nasal prongs, nasopharyngeal tube, or endotracheal tube).

・**Are there options for providing feedback to rescuers to ensure correct ventilation rates and tidal volumes?** Determine whether hyperventilation can be prevented during resuscitation.

Oxygenation

・**What are the safety and efficacy of supplementary oxygen provided during BLS?** For neonatal resuscitation, define optimal oxygen concentration during delivery room resuscitation (eg, room air versus oxygen-enriched air).

Pharmacological Interventions

・**Are vasopressin, epinephrine, or a combination of the 2 safe and effective for shock-resistant VF, pulseless VT, pulseless electrical activity, or asystole?** Identify optimal doses and timing of drug delivery and effects on postresuscitation organ function (if vasopressors are indeed effective). Consider novel and more selective vaso-

pressors (eg, &agr;-methylnorepinephrine) and pharmacological "cocktails" (eg, epinephrine and a &bgr;-adrenergic blocker).

・**Are antiarrhythmic drugs safe and effective for VF or pulseless VT?** Consider the effects of antiarrhythmic drugs on survival, including the safety and efficacy of the aqueous formulation of amiodarone.

・**Do &bgr;-adrenergic blocking agents improve survival from cardiac arrest?** Consider the effects of selectivity and duration of action.

・**Does administration of atropine during cardiac resuscitation improve outcome?** Consider dose-response effects on pulseless electrical activity and asystole.

・**Does administration of fibrinolytic agents and other agents that interfere with coagulation and blood clot formation during cardiac resuscitation improve outcome?** Consider origin of cardiac arrest (eg, pulmonary embolism, acute coronary syndrome).

・**Do agents that target pathways of ischemia and reperfusion injury improve survival from cardiac arrest?** Consider novel agents with preclinical supportive evidence, such as mitochondrial ATP-sensitive K^+ channel openers, opioid receptor agonists, Na^+-H^+ exchanger inhibitors, and growth factors such as erythropoietin and others.

・**What are the safety and efficacy of alternative routes of drug delivery (eg, endotracheal, intraosseous) during cardiac resuscitation?** Consider agents, dosing, overall effects on resuscitation interventions (eg, delayed intravenous drug delivery), and potential adverse pulmonary and hemodynamic effects in relation to underlying lung disease and age.

・**Does timing of drug delivery influence outcome?** Determine whether early drug administration (ie, before a defibrillation attempt) improves outcomes compared with current strategy (ie, after failure of initial resuscitation attempts).

Metabolic, Temperature, and Postresuscitation Management

・**What are the safety and efficacy of resuscitative and postresuscitative hypothermia?** Determine the influence of age (eg, neonate, child, and adult); optimal timing for initiation duration, and discontinuation of hypothermia; and optimal target temperature, Consider mechanism of arrest (eg, cardiac versus asphyxial arrest).

・**What is the optimal blood glucose concentration during and after resuscitation?** Determine whether tight glucose control improves outcome. Determine the optimal range of blood glucose concentration, methods of insulin administration, doses, indications, and end points. In neonates, assess the impact of early diagnosis of hypoglycemia and define blood glucose concentrations that may increase risk of brain injury after resuscitation.

・**Do vasoactive and inotropic agents given during the postresuscitation phase for myocardial dysfunction and hemodynamic instability improve outcome?** Determine agents, doses, indications, and end points.

・**What is the optimal temperature management for neonatal resuscitation in the delivery room (especially for preterm infants)?** Consider the effects of barriers to reduce heat loss from the head. Assess the effects of transparent membranes on heat exchange (eg, characterize evaporative, radiant, convective, and conductive heat gain and loss) and immature skin. Investigate the effects of hypothermia on long-term outcome in infants with encephalopathy. Determine the optimal depth and duration of hypothermia and the most effective method for initiating, maintaining, and discontinuing hypothermia.

Physiological Monitoring and Feedback

・**Do strategies for real-time physiological monitoring during CPR and the postresuscitation phase enable feedback for directive and/or corrective action, resulting in improved outcome?** Investigate the effect of continuous analysis of VF waveform, expired CO_2, depth and rate of compression, ventilation rate, and other measurements during CPR. Identify specific phases of cardiac resuscitation (eg, electrical, hemodynamic, and metabolic) to target priority interventions. Consider the effects of real-time feedback for directive and/or corrective action to optimize postresuscitation heart and brain function.

・**What is the impact of new technology developed to detect and quantify shock states?**

表3 Research Priorities in Acute Coronary Syndromes

Prehospital and Emergency Department Assessment
・What are the safety and efficacy of 12-lead ECG acquisition and computerized interpretation used by BLS providers to identify patients with STEMI?
Antiplatelet Agents
・Does a higher loading dose of clopidogrel offer additional benefit? Consider doses of 600 and 900 mg.
・What is the time-dependent efficacy of glycoprotein IIb/IIIa receptor inhibitors administered in the prehospital setting? Investigate safety of prehospital administration.
Heparin
・What are the safety and efficacy of prehospital and emergency department administration of unfractionated or low-dose low-molecular-weight heparin in unstable angina and NSTEMI?
・What is the optimal dose of low-molecular-weight heparin for prehospital and in-hospital care of patients with STEMI, balancing safety and efficacy in all age groups?
&bgr; -Adrenergic Blockers
・What are the safety and efficacy of prehospital and emergency department administration of &bgr;-blockers?
Reperfusion Strategies
・What are the safety and efficacy of PCI compared with fibrinolytic agents for patients with STEMI? Consider early presenters (ie, within 3 hours from onset of symptoms) and cost-effectiveness.
・What are the safety and efficacy of prehospital bypass to a facility with PCI capability?
・What are the safety and efficacy of community hospital fibrinolysis and transfer for PCI?
・What are the safety and efficacy of prehospital interventions (ie, 12-lead ECG and advance emergency department notification, fibrinolysis, or bypass to PCI site) on STEMI in rural and urban settings? Consider cost-effectiveness.

BLS indicates basic life support; STEMI, ST-segment-elevation myocardial infarction; NSTEMI, non-ST-segment-elevation myocardial infarction; and PCI, percutaneous coronary intervention.

表4 Research Priorities in Stroke

Stroke Centers
・What are the safety and efficacy of stroke centers?
・What are optimal criteria for transfer of hospitalized patients to a stroke center? Consider timing of transfer.
Pharmacological Interventions
・What are the safety and efficacy of blood pressure management m ischemic stroke?
・What are the criteria for risk stratification of patients considered for intravenous r-tPA? Assess age, timing, and blood pressure.
・Are there options for extending the 3-hour window for intravenous r-tPA? Consider novel methods for patient selection.
・What are the safety and efficacy of intra-arterial fibrinolysis and mechanical clot extraction in acute ischemic stroke?
Metabolic Management

・**What are the safety and efficacy of blood glucose control?** Consider timing, trigger level for implementing glucose control, target level, and duration.

・**What are the safety and efficacy of supplementary oxygen provided in acute stroke?** Consider normobaric and hyperbaric oxygen therapy.

Neuroprotective Therapies

・**What is the role of therapeutic hypothermia in acute stroke?** Consider timing, duration, degree, cooling method (eg, surface, endovascular, localized, or systemic), rate of rewarming, patient selection, and concomitant interventions (eg, recanalization, antiplatelet agents).

・**Can neuroprotective agents improve clinical outcome with and without concomitant recanalization strategies?** Consider novel agents with preclinical supportive evidence.

Transient Ischemic Attack

・**What are the criteria for risk stratification and admission and discharge decisions?**

Intracerebral Hemorrhage

・**What is the optimal method for managing intracerebral hemorrhage that occurs spontaneously or is associated with oral anticoagulation?** Consider optimal blood pressure management, metabolic management, and direct therapies for limiting hematoma and edema expansion.

r-tPA indicates recombinant tissue plasminogen activator.

PICO 方式での作成[1)]

Worksheet は資料を統一するために PICO に体系化した.

P＝Patient/Population

I＝Intervention

C＝Comparison

O＝Outcome

に沿って worksheet を提示することが求められる.

P は検討対象集団が広範か限定されてるか？worksheet にまとめられる母集団は多いほうがよい. たとえば, 心停止→院外心停止→院外心室細動と細分化して worksheet にまとめる.

Intervention/Comparison では Intervention が分析で最も大切である. 対照とする群は日常の治療(手技)または特別の治療群かを明記する.

Outcome は心停止に対する処置(Intervention)の終局の評価(予後)は生存(長期生存, 神経学的異常の残らない)とする. マネキンでの手技の評価などは例外であり, 手技が正確に行われたかの評価になる. **表5(1)(2)** に worksheet の作成例とこれに関与した evidence が positive, neutral, negative かについてそれぞれが level of recommendation に沿って示されていて客観的な判定が行いやすくなっている.

Intervention だけでなく, 診断, 予後が目的の worksheet もこの PICO 方式に従って作成される.

[文献検索法]

Cochrane Library, Medline, Embase さらに AHA で準備する Endonote Database が元になる. 検索した個々の論文の評価は次のようである.

①Level of Evidence

②Relevance to the question asked

③Methodological quality

④Outcome(s) assessed

⑤Magnitude of any observed effect

⑥Direction of support or otherwise for the hypothesis, according to the specific outcomes that have been assessed

この選んだ論文を①～⑥で分析して, worksheet の設問に対して個々の論文につき以下を示す.

①support, neutral, negative のいずれかを判断する.

②Level of Evidence の評価

③Quality of Study の評価

④Outcomes assessed の評価

表5(1) に worksheet のサンプルを示してあるが, Hypothermia の worksheet であるが, これを作成してそれを基にして**表5(2)**のような評価表が完成されることになる.

図3 に worksheet の完成されるまでの流れを示すが，2005年に比べ作業が簡単になり，作成された worksheet の評価が reviewer により check されるが，この作業も客観的に行えるようになった．Worksheet author が完成したのを Worksheet Expert Reviewer が評価して，author に改訂を求める場合もある．最後に E3 が認めたのが，Task Force Chairs に送られ再度評価を受ける．こうして個々での評価で可とされた worksheet が C2010 Conference（Ghent）で全員からの評価を受ける．これではじめて CoSTR の作成の資料となる．2010年に入り CoSTR Editorial Board によりこれが lock on され，最終版の CoSTR 2010 として出版されことになる．

Table 5（1）　Example of worksheet: Induced hypothermia[1)]

WORKSHEET for Evidence-Based Review of Science for Emergency Cardiac Care **Worksheet author（s）**	
Peter Morley, Jerry Nolan	**Date Submitted for review:** 4 April 2006
Clinical question.	
Does the use of induced hypothermia（I）improve survival（O）in patients after cardiac arrest（P）? **Is this question addressing an intervention/therapy, prognosis or diagnosis:** Intervention/therapy. **State if this is a proposed new topic or revision of existing worksheet:** Revision	
Search strategy（including electronic databases searched）.	
PubMed "heart arrest" or "cardiopulmonary resuscitation" as MESH（headings）AND "Hypothermia" textword in abstract. EMBASE search using text words（all fields）hypothermia AND（cardiac arrest OR resuscitation） AHA EndNote Master library, Cochrane database for systematic reviews, Central Register of Controlled Trials, Review of references from articles.　Forward search using SCOPUS and Google scholar.	
・State inclusion and exclusion criteria The following studies were excluded: Not true cardiac arrest models（eg. exsanguinations, great vessel occlusion[x], carotid artery occlusion[y]）, pre-arrest[z] or during arrest cooling[a], resuscitation with cardiopulmonary bypass instead of CPR[b], reports of single cases.	
・Number of articles/sources meeting criteria for further review: 28 studies met criteria for further review.　Of these 5 were LOE 1（RCTs）, two LOE 2（non-randomised, concurrent controls）, two LOE 3（retrospective controls）, eight LOE 4（no controls）, and eleven LOE 5（not directly related; all animal studies）.	

Table 5（2）　Example of worksheet: Induced hypothermia

Summary of evidence
Evidence Supporting Clinical Question

Good	Hypothermia After Cardiac Arrest Study Group, 2002 CD*				*Hicks, 2000 DE*
Fair					*Agnew, 2003 DE* *D'Cruz, 2002 E* *Horn, 1991 E*
Poor	Hachimi-Idrissi, 2001（1）E Tiainen, 2003 E*	Bernard, 2002 CD	Bernard, 1997 D	Bernard, 2003 E Williams, 1958 D	
	1	2	3	4	5
Level of evidence					

A＝Return of spontaneous circulation　C＝Survival to hospital discharge　E＝Other endpoint
B＝Survival of event　D＝Intact neurological survival　*Italics＝Animal studies*
*＝overlapping patients

Evidence Neutral to Clinical Question

Good					*Hachimi-Idrissi, 2001 (2) DE* *Katz, 2004 (1) E* *Sterz, 1991 E*
Fair	Zeiner, 2004 E Callaway, 2002 E		Yanagawa, 1998 CDE		*Katz, 2004 (2) E* *Mullan, 1961B* *Wolfe, 1960 B* *Xiao, 1998 E*
Poor		Benson, 1959C		Al-Senani, 2004 CDE Felberg, 2001 Nagao, 2000 Sanada, 1998 Silfvast, 2003 Zeiner, 2000	
	1	2	3	4	5
Level of evidence					

A＝Return of spontaneous circulation　C＝Survival to hospital discharge　E＝Other endpoint
B＝Survival of event　D＝Intact neurological survival　*Italics＝Animal studies*

Evidence Opposing Clinical Question

Good					
Fair			Yanagawa, 1998 E		
Poor					
	1	2	3	4	5
Level of evidence					

A＝Return of spontaneous circulation　C＝Survival to hospital discharge　E＝Other endpoint
B＝Survival of event　D＝Intact neurological survival　*Italics＝Animal studies*

ここで C2005 と C2010 での worksheet 作成での区別した点を英語のまましめす.

C2005[1)]
Plan for 2 (at least one) authors (AHA/non?)
Sometimes more than 2
Sometimes only 1
Enormous variability in quality/timeline
・Commitment to process/timeline
・Knowledge of goal of worksheet
・Skill in evaluation
Variable outcomes
Separate, joint, combined summary

C2010
Revision of old worksheet
Previous reviewers become default (?)
But screened (for previous completed product)
New worksheet
Taskforce, volunteers (councils)
New (or old) reviewers should have 'mentor' (early) to deal with minor issues
Taskforce co-chairs (Nominator?)
Ideal plan (default) still 2 authors/worksheet
Best for systematic review process
"Agreed search strategy, and articles found
"Independent review of articles to exclude
"Independent methodological assessment
"Combined summary
"Combined COS
"Combined TR
In general, one starts and other edits

One will do more work that the other

診断，予後に関する worksheet

Intervention だけでなく診断，予後についても worksheet が以下の原理で作成される．

Studies of diagnostic tests

"Test"＝examination finding/investigation

Gives "result"

Starting point is initial "test" on patients

Compare "test" result with known outcome ("gold standard")

Develop threshold result (to alter Mx) ＝ Clinical Decision Rule (CDR)

Better＝confirm result in multiple centers

C2010 LOEs for Diagnostic Studies

LOE1: Validating cohort studies (or meta-analysis), or Validation of Clinical Decision Rule (CDR)

LOE2: Exploratory cohort study (or meta-analyses), or derivation of CDR, or split-sample validation only

LOE3: Diagnostic case control study

LOE4: Study of diagnostic yield (no reference standard)

LOE5: Studies not directly related to the specific patient/population (eg. Different patient/population, animal models, mechanical models etc)

LOE D1 の例を示す．

In a group of consecutive patients with VF from multiple settings, a previously determined Clinical Decision Rule was confirmed to predict increased likelihood (＋LR＝12) of ROSC after shock.

LOE D2 の例を示す．

In a group of non-consecutive patients with VF, a specific cut off point could be determined that predicted increased likelihood (＋LR12) of ROSC after shock. This was determined in 50% of patients and validated in the other 50%.

予後に関する worksheet に関しては以下の点が示された．

Studies related to prognosis

All "prognosis" questions share 3 elements

a qualitative aspect (which outcomes could happen?)

a quantitative aspect (how likely are they to happen?), and

a temporal aspect (over what time period?)

Starting point is assessing factor on patients

Compare relation of presence or absence of factor to outcome

(Develop Clinical Decision Rule (CDR) eg. combination of multiple factors)

Best＝confirm result in multiple centers

が原則であり，C2010 での予後 LOE として以下の提案がなされた．

C2010 LOEs for Prognostic Studies

LOE P1: Inception (prospective) cohort studies (or meta-analyses of inception cohort studies), or validation of Clinical Decision Rule (CDR)

LOE P2: Follow up of untreated control groups in RCTs (or meta-analyses of follow-up studies), or derivation of CDR, or validated on split-sample only

LOE P3: Retrospective cohort studies

LOE P4: Case series

LOE P5: Studies not directly related to the specific patient/population (eg. different patient/ population, animal models, mechanical models etc)

ま と め

CoSTR2010 の作成作業は ILCOR が総力を挙げて取り組んできた．2005 以降の new data と 2005 でとりあげなかった Gaps knowledge と 2005 での問題も再検討する 3 通りの分析により，精度の高い世界の文献が網羅されていて，これからの ILCOR 会議で輪郭がよりはっきりすることになる．Orlando の会議はその基礎を十分理解するのに大変有益であり，CoSTR 2010 が多くの人の大変な努力で進んでいる現状を説明した．英語のままの説明を残したのも CoSTR 会議の臨場感をできるだけ伝えたいと思ったからである．まだ 2010 までに間に合うので日本，アジアからの evidence がこの作成にたくさん加わることを願っている．

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